FEBRUARY, 1953

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Clinical Evaluation of the Common Bile Duct Postoperatively

Significant Factors in the Etiology of Gastrojejunal Ulcer

A Case of Gumma of Liver Diagnosed by Liver Biopsy

Some Interesting Experiences with Jaundice

•

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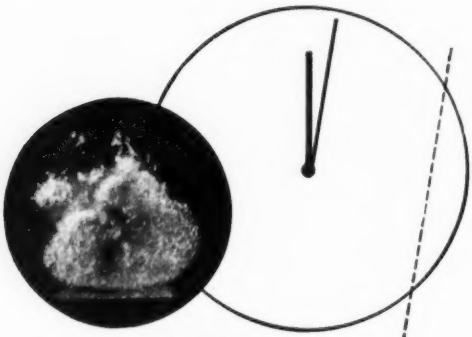

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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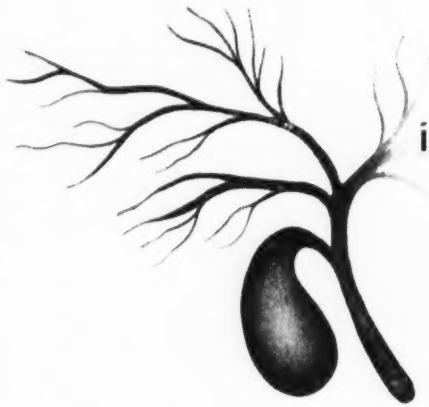

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The Review of Gastroenterology

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Volume 20 FEBRUARY, 1953 Number 2

CLINICAL EVALUATION OF THE COMMON BILE DUCT, POSTOPERATIVELY

JULIAN A. STERLING, M.D., D.Sc. (Med.), F.A.C.S.
Philadelphia, Pa.

Clinical evaluation of the common bile duct following choledochostomy is obtained in several ways. First, the patient's response is observed after the "T" tube has been closed; second, the appearance of the duct is studied on cholangiogram; and third, intracholedochal pressures and volumes are measured[2] with particular attention directed to the response to added measured fluid[5].

The patient who tolerates a closed "T" tube for 72 hours without pain, jaundice, chills or fever does not need the tube and usually has a patent common bile duct. In addition, free flow (of "Diodrast") into the duodenum and the radiographic evidence of normal contours and course of the common duct indicate a normally functioning common bile duct. Measurement of the volume contained within the common bile duct and of pressure variations within it are valuable in determining the status of the common bile duct.

There are certain defects inherent in all these methods. Accordingly, my experiences with measurement of intracholedochal pressures and volumes, as relate to pertinent clinical features, have been reviewed. As a result of these studies, it is found that any single test is not fully reliable.

Procedures

Sixteen complete representative case studies have been selected from more than one hundred studies to date. These sixteen patients had from two to five years "follow-up" observation, except for case sixteen who is now only one year postoperative.

Investigations were conducted on patients after various surgical procedures relating to the common duct. Operative, cholangiographic and clinical observations were recorded in inflammatory, calculous, traumatic and malignant disease

From the Surgical Service of the Albert Einstein Medical Center (Northern Division) Philadelphia, Pa.

of the common duct. Direct, operative, cholangiograms were done with 70 per cent "Diodrast" through a (ureteral) catheter (or "T" tube) in the cystic or common bile duct. Indirect, postoperative, cholangiograms, usually under fluoroscopic control, were done using 35 per cent "Diodrast" through the external limb of the indwelling "T" tube[8].

In all cases, the "T" tube was examined to assure free flow within its lumen prior to common duct intubation. Care was used in placing the tube to avoid angulation or compression. The "T" tube drainage was measured daily. As the volume of daily drainage decreased below 300 cubic centimeters (and usually after the fourth day), the tube was clamped for intervals ranging from one to three hours. At the conclusion of one of these intervals when the tube had been clamped, a three-way stopcock was attached to the external opening of the "T" tube placed approximately at the level of the common bile duct in the sagittal plane of the body. A 20 cubic centimeter syringe and a water manometer were also attached to the three-way stopcock. The water manometer was filled with physiological saline solution. The pressure in the common bile duct was then measured and the intracholedochal contents measured. Five to ten cubic centimeter quantities of one per cent novocaine or physiological saline solution were then injected into the "T" tube each minute. Usually, from 15 to 30 cubic centimeters of fluid were injected into the common duct during a period of five minutes. Light pressure was exerted against the syringe plunger. Measurements of intracholedochal pressures were recorded at 30 to 60 second intervals.

After an observation period lasting about ten minutes, the common duct was aspirated; volume and pressure measurements were again recorded. This examination was repeated after a rest period of five or more minutes during which the external limb of the "T" tube had been clamped. Clinical observations were noted regarding nausea, abdominal distress and site and character of any pain. On occasion, papaverine (hypodermically) or nitroglycerin (sublingually) were administered in therapeutic dosage.

Pressure and volume changes within the duct were recorded. A statement was inserted on the clinical record regarding the common bile duct, such as, "normal" or "calculous". The following were then correlated:

1. Measurements of intracholedochal pressures and volumes.

2. Cholangiogram.

3. Clinical course of the patient.

The typical pressure and volume responses observed in the normal and abnormal common bile duct are illustrated in Figure 1. Similar graphs were prepared in each case. An indirect cholangiogram was usually done the day after this study because the measurement of intracholedochal pressure and volume usually added air to the biliary tract.

Case Reports

A. *Patients with a normal common bile duct.*

Case 1:—(S. W., 41, female) This patient was admitted to the hospital because of intolerance to fatty foods of 20 years' duration. There had been recent increase of abdominal pain. No jaundice.

Cholecystectomy was done for chronic calculous cholecystitis. A dilated common duct was explored. It was not abnormal. The papilla was probed with an ureteral catheter. Injected fluid entered the duodenum easily. Operative cholangiogram was normal.

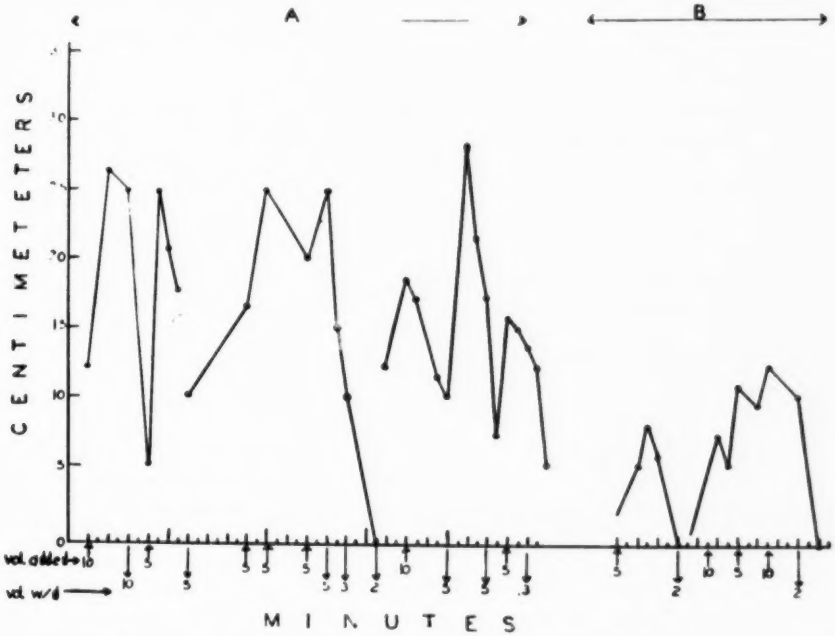

Fig. 1—Graphic record of normal (B) and abnormal (A) intracholedochal pressures and volumes.

Intracholedochal pressure study was done eight days postoperatively. Findings were as follows: residual volume and pressure were zero; injection of 10, 15 and 30 cubic centimeters of solution raised the intracholedochal pressure to 8, 10 and 15 centimeters of water. The common duct emptied at an average rate of seven cubic centimeters per minute. At different times under different conditions, the duct emptied at from two to eleven cubic centimeters per minute. This was normal.

Cholangiogram done eleven days postoperatively was normal. The patient was asymptomatic when the "T" tube was clamped and has been fully comfortable since its removal.

Conclusion:—Pressure study, cholangiogram and clinical course agree.

Case 2:—(M. G., 41, female) This patient was admitted to the hospital because of a four-year history of abdominal pain and associated gastrointestinal disturbances.

Cholecystectomy was done for chronic calculous cholecystitis. The common duct was explored because it was enlarged. The common duct was normal.

Intracholedochal pressure was studied ten days postoperatively and revealed a rise in pressure to a maximum of 19 centimeters of water. The emptying rate of the duct was ten cubic centimeters per minute.

An indirect cholangiogram was normal. The patient was asymptomatic when the "T" tube was clamped and has been well since its removal.

Conclusion:—Clinical course, intracholedochal pressures and cholangiogram all agree.

Case 3:—(S. K., 64, female) The patient was admitted to the hospital because of abdominal pain of five days' duration with associated digestive disturbances of one year's duration. There was no history of jaundice, but it did appear on the day after admission. This patient had only fair cardiac function in addition to moderate thyrotoxicosis. She was prepared for surgery. Cholecystectomy was done for chronic calculous cholecystitis. The common duct was explored, irrigated and found to be normal.

Because the patient had a stormy postoperative course, intracholedochal pressure studies were not done until 37 days postoperatively. Maximal intracholedochal pressure rose only to 11 centimeters of water. The emptying rate of the duct was six cubic centimeters per minute.

The cholangiogram done the following day was normal. No cause was found in the biliary tract for the pre-existing jaundice. Following the clamping of the "T" tube, the patient was completely asymptomatic and has remained well after the removal of the tube.

Conclusion:—Cholangiogram, pressure studies and clinical course agreed in this patient.

Case 4:—(C.J., 54, female) This patient was admitted to the hospital because of gastrointestinal symptoms of four years' duration.

Cholecystectomy was done because of chronic calculous cholecystitis. The common duct was dilated and hence was explored. Fluid entered the duodenum readily. Operative cholangiogram was not done in this case.

Pressure study was done on the common bile duct six days postoperatively. The residual pressure and volume in the common duct were zero. Injection of fluid into the duct in increasing quantities did not increase pressure beyond 15 centimeters of water. The emptying rate of the duct was ten cubic centimeters per minute.

Conclusion:—Cholangiogram, pressure studies and clinical course were all normal.

Case 5:—(O.J., 22, male) The patient was admitted to the hospital complaining of severe abdominal pain of two days' duration. The diagnosis of pancreatitis was made. The blood amylase was 4,500 units (Somogyi). Icterus index was 50 units.

Two weeks after admission, cholecystectomy was done because of chronic calculous cholecystitis. The pancreas was edematous. Several small stones were found in the cystic duct. Exploration of the common duct was normal in that fluid was readily injected into the duodenum. The gallbladder was removed and the common duct was drained. Operative cholangiogram could not be done in this case because of technical deficiencies.

Pressure studies were normal nine days postoperatively. A cholangiogram done ten days postoperatively was normal. After clamping the "T" tube, the patient was asymptomatic for 24 hours. The clinical course of this patient, subsequently, was normal.

Conclusion:—Pressure study, cholangiogram and clinical course agree.

B. Patients with residual choledocholithiasis.

Case 6:—(C.R., 26 female) Operation was done because of cholelithiasis coincident with a history of persistent, slight jaundice. After the common duct was explored, cholecystectomy was done. A stone was not found in the common duct and the fluids injected into it rapidly entered the duodenum. Operative cholangiogram was not fully satisfactory except that it indicated the presence of the radio-opaque dye in the duodenum.

The "Best"[1] type of double-lumen "T" tube was placed in the common duct and drained continuously for 48 hours. On the third day, the tube was closed for two-hour intervals; and on the fourth day the tube was opened for two-hour intervals. On the fourth postoperative day there was some discomfort in the abdomen which resembled preoperative symptoms.

Intracholedochal pressure and volume studies were done on the fifth postoperative day. Initial intracholedochal pressure was 14 centimeters of water. Residual duct volume was nine cubic centimeters. The introduction of ten cubic centimeters of one per cent novocain into the duct was followed immediately by moderate pain and an increase in the intracholedochal pressure to 26

centimeters of water. The duct did not empty the fluid into the duodenum; the duct pressure was maintained until all the injected fluid had been withdrawn.

Two cubic centimeters of nupercaine were then injected into the duct. After ten minutes, two cubic centimeters of ether were instilled, drop by drop, into the "T" tube. The external limb of the "T" tube was clamped for 30 minutes. The duct was then washed with generous quantities of one per cent novocain solution. Much debris consisting of orange colored biliary sand was washed from the duct. Further lavage was clear.

Subsequently, there was no pain associated with determinations of pressure and volumes within the common duct. During later studies, instillation of five to twenty cubic centimeters of solution provoked pressures only up to 14 centimeters of water and the duct was found to empty at a rate of three to five cubic centimeters per minute. Figure 1 illustrates the changes observed in the intracholedochal pressures and volumes.

Indirect cholangiogram in this patient showed a residual dilatation of the duct without, however, any sign of calculous. The "T" tube was clamped for 48 hours without adverse effect.

Following removal of the "T" tube, the duct fistula closed rapidly and the patient has been asymptomatic.

Conclusion:—Cholangiogram, pressure study and clinical study agree.

Case 7:—(H.C., 40, female) The patient was admitted to the hospital because of abdominal pain of four weeks' duration. Cholecystectomy was performed because of chronic calculous cholecystitis. Choledocholithotomy was done to remove two calculi.

The common duct was studied six days postoperatively. Pressure (10 centimeters) and volume (15 centimeters) readings at beginning of observations were elevated. After aspirating the duct, ten cubic centimeters of fluid were injected into the duct; this raised the intracholedochal pressure to 18 centimeters of water. The emptying rate of the duct was three cubic centimeters per minute. Injection of 20 cubic centimeters of fluid raised the pressure to 27 centimeters of water. The emptying rate of the duct was six cubic centimeters per minute. These results were within normal limits when it was considered that this was a post-calculous common bile duct.

A cholangiogram done eight days postoperatively, however, revealed radio-opaque shadows in the duct which resembled calculi. Cholangiogram was repeated 13 days postoperatively. At this time, the abnormal shadows were absent. Pressure studies were unchanged. The "T" tube was clamped for 48 hours and then removed. The patient has been asymptomatic since.

Conclusion:—The clinical course, including the pressure studies, indicated normalcy. The first cholangiogram was doubtful, possibly because of redundant

mucosal folds, secondary to choledocholithiasis and operative trauma. The disappearance of the abnormal shadows and the subsequently normal cholangiogram confirmed the pressure studies. Since the subsequent clinical course was normal, it must be assumed that the common duct was normal postoperatively.

Case 8:—(A.C., 33, female) This patient was admitted to the hospital because of abdominal pain of one year's duration, associated with digestive disturbances.

Cholecystectomy was done because of chronic calculous cholecystitis. Choledocholithotomy was done to remove multiple small stones. Irrigating fluid passed rapidly into the duodenum. Operative cholangiogram was not done.

Studies done seven days postoperatively indicated a residual pressure of six centimeters and a residual common duct volume of six cubic centimeters. Introduction of volumes up to 20 cubic centimeters raised intracholedochal pressure only to 14 centimeters of water. Emptying rate of the duct was five cubic centimeters per minute. This behaved like a normal duct except for evidence of preexisting dilatation.

A cholangiogram was done two weeks postoperatively. This indicated a radio-opaque shadow to be present at the termination of the common bile duct. Pribram[6] therapy was administered for five days, at which time cholangiogram showed a normal duct. The closed "T" tube was permitted to remain in the duct for three months. At the end of that time, the tube fell out. The patient has been asymptomatic ever since.

Clinical course and pressure studies agreed that the duct was functioning. The cholangiogram, however, indicated the possible presence of a calculous. This shadow disappeared coincident with conservative management.

In this case, the patient was clinically normal during all postoperative phases. Although an early postoperative cholangiogram indicated an obstruction, a later cholangiogram was perfectly normal.

Conclusion:—Lack of agreement in this case between clinical findings and the obstruction seen on cholangiogram may have indicated the presence of damaged mucosa in the papillary portion of the common bile duct.

Case 9:—(C.H., 80, female) This patient was admitted to the hospital because of abdominal pain of 40 years' duration and intermittent jaundice of ten years' duration.

Cholecystectomy was done because of chronic calculous cholecystitis. Exploration of the common duct revealed ten stones to be present, each approximately 1.5 centimeters in diameter. Because of the poor risk in this case, operative cholangiogram was not done.

Common duct pressure was studied five days postoperatively. The residual volume of the duct was approximately thirty cubic centimeters. Intracholedochal

pressure in the resting state ranged from ten to 18 centimeters of water. Addition of fluid to the duct was painful and pressure rose abruptly after fifteen cubic centimeters had been introduced. The emptying time of the duct was one cubic centimeter per minute. This study indicated the presence of obstruction to duct emptying coincident with a large residual volume of duct. The cholangiogram which was done one week postoperatively showed the presence of two residual common duct stones. Pribram therapy[6] was continued for two weeks.

The residual volume continued at 30 cubic centimeters. Upon addition of 35 cubic centimeters of fluid, pressure rose from zero to 32 centimeters of water. The emptying time of the duct remained at one cubic centimeter per minute. Pain was present whenever the intracholedochal pressure rose above 20 centimeters of water. Cholangiogram showed that the stones persisted. Choledocholithotomy was done six months later with success.

Conclusion:—Pressure study, cholangiogram and clinical course agreed on the presence of obstruction in the common duct.

Case 10:—(S.W., 62, female) This patient was admitted to the hospital because of 15 months' severe right upper quadrant pain. There was no history of jaundice.

Cholecystectomy was done for chronic calculous cholecystitis. The common duct was explored and several stones removed from it. Unfortunately, operative cholangiogram could not be done.

Common duct pressure was studied ten days postoperatively. Residual pressure varied between zero and ten centimeters of water. The residual duct volume was five cubic centimeters. The injection of fluid into the duct was accompanied by pain. This pain was maximal at 24 centimeters of water pressure. Fluid could not be added to the system above this level. The emptying rate of the duct was one to two cubic centimeters per minute.

A cholangiogram showed two stones remaining in the common bile duct. Conservative therapy was utilized[7]. After two weeks of treatment, there was no change in the patient except that intracholedochal pressure rose to 28 centimeters of water. These stones were removed from the common duct eight months later.

Conclusion:—Pressure study was doubtfully positive, cholangiogram was positive and clinical study was positive.

Case 11:—(F.R., 76, female) This patient was admitted to the hospital because of abdominal pain of 20 years' duration.

Cholecystectomy was done for chronic calculous cholecystitis. The common duct was opened beause it was dilated. Sand and minute stones were present. Direct cholangiogram was not done.

Common duct pressure and volume studies were done three weeks postoperatively. Residual pressure in the common duct was zero to six centimeters of water. Residual volume of the duct varied from two to eight cubic centimeters. The duct emptying rate was one cubic centimeter per minute. Intracholedochal pressure did not rise beyond 18 centimeters of water.

Cholangiogram revealed a stone to be present in the distal portion of the extraduodenal common duct. Patient did not tolerate Pribram therapy. Exploratory operation was performed six weeks following the original procedure. The common duct stone was removed. Pressure-volume studies and cholangiography following this operation were not done because the patient's postoperative status was precarious. "T" tube remained in place though clamped after one week. Since the patient was free from symptoms, the tube was removed. The patient had a myocardial infarct and died two years later.

Conclusion:—Common duct pressure, cholangiogram and clinical course agreed.

Case 12:—(F.K., 54, female) This patient was admitted to the hospital because of severe abdominal pain and indigestion of 36 hours' duration. Diagnosis was made of pancreatitis and cholelithiasis. The patient was prepared preoperatively for two weeks. Cholecystectomy was done because of gangrenous cholecystitis, secondary to chronic calculous cholecystitis. Fat necrosis was present. The common duct was opened and eight small calculi were removed. Following the use of Bake's dilators and the passage of soft rubber catheters, the duct appeared to be unobstructed to the flow of fluid. A "T" tube was sewn in place.

The postoperative cholangiogram indicated that a residual calculous was present in the common bile duct. After six months of intermittent Pribram therapy, a cholangiogram revealed that the stone was still present.

Intracholedochal pressures and volumes were measured on several occasions. Residual pressure was six centimeters of water. Residual volume varied from 10 to 15 cubic centimeters. With the introduction of 5, 10 and 15 cubic centimeters of solution, intracholedochal pressures rose to 15, 30 and 32 centimeters of water pressure respectively. Pain was present at 25 centimeters of water. The duct emptied at a rate of two cubic centimeters per minute but did not empty completely since residual volumes of 11 to 15 cubic centimeters were obtained at the end of 10 to 15 minute rest periods.

The patient continued on therapy with ether instillations in accordance with the Pribram routine for another four months[6]. At the end of that time, a study of the intracholedochal pressures and volumes was repeated. There was no residual fluid in the common bile duct and initial pressure was zero centimeters of water. The duct emptied eight to nine cubic centimeters per minute and at the end of five minutes, there was no residual fluid within the common bile duct. At this time, the intracholedochal pressure was zero. Cholangiogram at this time visual-

ized an uninterrupted flow of Diodrast into the duodenum and no evidence of calculi. Her clinical course since the removal of the "T" tube has been fully asymptomatic to the present.

Conclusion:—Common duct pressures, cholangiograms and clinical states agreed.

C. Patients with marked edema or spasm of the papilla.

Case 13:—(A.R., 54, female) This patient was admitted to the hospital because of abdominal pain of six months' duration. Cholecystectomy was done because of chronic calculous cholecystitis. Since the common bile duct was dilated, it was opened. No stone nor other abnormalities were found within it. Operative cholangiogram was not done.

Pressure studies were done seven days postoperatively. Resting pressure in the common bile duct was eight centimeters of water. Residual volume in the common duct was five cubic centimeters. Addition of 10, 15 and 20 cubic centimeters of solution raised pressure rapidly to 18, 25 and 30 centimeters of water. Emptying rate of the duct was three cubic centimeters per minute. Intraductal pressure did not fall below six centimeters of water at any time. The increased residual volume and pressure, together with slow emptying, indicated that incomplete obstruction due to sphincter spasm or edema were present. Studies done seven days postoperatively showed that the intracholedochal pressure rose to 30 centimeters of water. Pressure studies done 12 days postoperatively indicated a rise only to 18 centimeters of water.

The cholangiogram done eight days postoperatively indicated radiolucent shadows at the termination of the common bile duct. Cholangiogram repeated 13 days postoperatively was normal. Clamping of the "T" tube for 48 hours was asymptomatic. The tube was removed; the patient has since been healthy.

Conclusion:—The clinical course and pressure studies indicated spasm or edema of the common duct sphincter to be present. Organic obstruction was not suspected since the duct emptied slowly and regularly. This was confirmed since the first cholangiogram showed shadows which in hind-sight represent redundant mucous membrane. The second cholangiogram was completely normal.

Early studies did not agree, although the patient was comfortable. Between the eighth and thirteenth days, the termination of the common bile duct returned to normal. The later studies all concur.

Case 14:—(J.K., 46, female) This woman was admitted to the hospital complaining of eight years' fatty food intolerance and abdominal pain without jaundice.

The gallbladder was removed because of chronic calculous cholecystitis. The common duct was explored but no stones were found. Operative cholangiogram was not done.

Postoperative pain was present when the tube was clamped. Bile leaked around the "T" tube.

Pressure study, six days postoperatively, revealed an emptying time of one cubic centimeter per minute and intracholedochal pressure up to 14 centimeters of water. Pressure study repeated ten days postoperatively revealed the same emptying rate but the pressure rose to 22 centimeters of water. A cholangiogram done 11 days postoperatively revealed a radio-opaque shadow resembling a stone present at the distal end of the extraduodenal common duct.

Pribram therapy was started but was not well tolerated by the patient. At re-operation, three weeks later, a stone was not found. Pressure study done eleven days following the second operation revealed an emptying time of one cubic centimeter per minute. Intracholedochal pressure rose to 18 centimeters of water. A cholangiogram revealed the same shadow as seen in the first postoperative radiograph.

The "T" tube fell out after being clamped for three months. The patient is symptomatic with pain and indigestion. The patient has continued to have indigestion for the past two and one-half years.

Conclusion:—An unidentified shadow on the cholangiogram in the distal end of the common duct produced partial obstruction clinically and delayed emptying of duct along with increased residual volume and maintained elevation of intracholedochal pressure. All these studies agree.

Case 15:—(H.G., 75, male) This patient was admitted to the hospital complaining of abdominal pain of many years' duration.

Cholecystectomy was done for chronic calculous cholecystitis. Choledochotomy was done because the common duct was dilated. There were no abnormal findings. Injected fluid entered the duodenum readily. Bake's dilators[11] were passed. Direct cholangiogram was normal.

Common duct pressure studies were done five days postoperatively. Residual volume of the duct was zero. Emptying rate of the duct was three cubic centimeters per minute. Intracholedochal pressure ranged from zero to 31 centimeters of water with the addition of increased volumes into the duct.

Cholangiogram revealed a doubtful radiolucent shadow in the duct. During his postoperative course, however, there was neither pain nor jaundice. The "T" tube was clamped without symptoms. Following removal of the tube, the patient has remained asymptomatic.

Conclusion:—Pressure studies were normal. Cholangiogram was doubtful; clinical course of the patient indicated a normal duct. The lack of correlation placed doubt on the significance of the radiographic observation in this case.

D. Tumor of the papilla of Vater.

Case 16:—(J.K., 58, male) The patient was admitted to the hospital because of obstructive jaundice of three weeks' duration.

At operation, the gallbladder was distended and the liver was enlarged because of biliary cirrhosis. All tissues were icteric. There was no other obvious abnormality.

A small tumor was palpated at the papilla of Vater[10]. The papilla was then removed at about one and one-half centimeters proximal to the tumor (bile duct carcinoma) by transecting the common bile and pancreatic ducts. The ducts were re-implanted. A "Cattell"-type "T" tube was placed through the common duct into the duodenum. (This case will be reported in detail when a sufficient interval has elapsed.)

The significance of this case in mechanical physiology of the biliary tract is in the complete obstruction to the common bile duct in the absence of any other disease. Examination of the papilla of Vater revealed two separate orifices and a papilla which, except for the tumor, was identical with the normal specimens described previously[9].

Pressure-volume studies were done in this patient on the tenth postoperative day. Residual volume and pressure were both zero. Fluid injected into the external limb of the "T" tube was discharged intraduodenally at the rate with which it was injected. There was no obstruction to flow nor any sphincter effect. Cholangiogram was not done. The "T" tube was clamped shut for three months after which it was removed.

Conclusion:—Free flow and asymptomatic clinical course were significant of return to normal dynamics in the absence of a papilla.

Discussion

Among the sixteen patients herein reported, five were found to have a normal common bile duct, seven had residual calculi in the common bile duct, and three had evidence of edema or spasm of the papilla of Vater. In the seven who had residual stones in the common bile duct, re-operation was necessary in three. One patient may require re-operation.

In three cases, the stones passed spontaneously or in association with some method of Pribram therapy.

Correlation of the results of 22 studies have been tabulated (Table I). Of these, 18 (or 82 per cent) presented accurate agreement among the pressure and volume studies, the cholangiogram and the clinical responses.

In four cases, the three "test" factors were not correlated. In two of these cases, there were abnormal shadows present on cholangiogram, while studies

of pressures and volumes within the common duct and the clinical response secondary to clamping the tube demonstrated that the duct was functioning normally. In these two cases, re-examination indicated that the shadow seen in the common bile duct was probably due to distortion of the common bile duct mucous membrane. This could have been secondary to the trauma produced by exploration with metallic probes[11]. In these two cases, subsequent studies indicated that the interpretation of the cholangiogram was in error.

TABLE 1

CORRELATION OF STUDIES ON THE COMMON BILE DUCT

Case Number Clinical Diagnosis	Pressure Volume Studies	Cholangiogram	Clinical Test	Correlation
(1) Normal common duct	Clear	Clear	Clear	Yes
(2) Normal common duct	Clear	Clear	Clear	Yes
(3) Normal common duct	Clear	Clear	Clear	Yes
(4) Normal common duct	Clear	Clear	Clear	Yes
(5) Pancreatitis	Clear	Clear	Clear	Yes
(6) Residual stone which passed	a. Obstruction	Dilatation	Obstruction	Yes
	b. Clear	Clear	Clear	Yes
(7) Stones	Clear	Shadow	Clear	*No*
(8) Stones and edema of papilla	a. Clear	Shadows	Clear	*No*
	b. Clear	Clear	Clear	Yes
(9) Stones	Obstruction	Obstruction	Obstruction	Yes
(10) Stones	Partial obstruction	Obstruction	Obstruction	Yes
(11) Stone	Partial obstruction	Shadow	Obstruction	Yes
(12) Stone	a. Obstruction	Shadow	Obstruction	Yes
	b. Clear	Clear	Clear	Yes
(13) Edema	a. Partial obstruction	Shadows	Clear	*No*
	b. Clear	Clear	Clear	Yes
(14) Edema of papilla	a. Partial obstruction	Shadow	Partial obstruction	Yes
	b. Partial obstruction	Shadow	Partial obstruction	Yes
(15) Edema of papilla	Clear	Shadow	Clear	*No*
(16) Tumor	Clear	Not done	Clear	Yes

In the other two cases of disagreement among the three "test" factors, the common bile duct function was clinically normal when the tube was clamped although a shadow was present on cholangiogram. In these, there was an abnormal pressure-volume study. In one of these cases, a stone was surgically removed from the common bile duct while in the other case the abnormality disappeared spontaneously.

The residual volume of the normal common bile duct ranged up to five cubic centimeters of water. This varied because of a variable base-line which included factors such as food-stimuli, state of tonus of the duodenum, content of the duodenum, intraperitoneal pressure and the patient's state of mind[2,3]. Residual volumes greater than seven cubic centimeters, however, were associated with some obstruction at the termination of the common bile duct.

The normal "resting" pressure of the common bile duct ranged up to five centimeters of water. When the residual pressure was greater than ten centimeters of water, either a calculus was present or there was edema or a flap of redundant mucosa at the papilla.

As fluid was injected into the duct, it was found that intracholedochal pressure rose in a ratio of one, or one and one-half, to one until a maximal pressure of 15 to 18 cubic centimeters of water was present following the instillation of 10 to 15 cubic centimeters of solution. At this level, the patient would complain of moderate discomfort and a sense of abdominal fullness. This was relieved as the intracholedochal pressure decreased.

The duct volume normally decreased at the rate of three to five cubic centimeters per minute. The normal duct returned very quickly to its original volume and pressure.

The duct, which presented an obstruction due to a calculus, varied in three categories:

1. If the life history of the stone were short, the volume content of the duct was less than 15 cubic centimeters, whereas the pressure within the duct frequently ranged between 25 and 30 centimeters of water. This duct emptied slowly, or not at all, depending upon the location of the calculus.

2. When the life history of the stone was of many months, the volume content of the duct was usually greater than fifteen cubic centimeters, whereas the intracholedochal pressure was less than 25 centimeters of water. This duct usually emptied slowly.

3. The duct which had once contained a calculus (either removed surgically or spontaneously passed) presented a volume greater than 15 cubic centimeters with a low pressure (usually not over 10 centimeters of water) and which emptied rapidly (10 cubic centimeters per minute).

In patients who had edema due to trauma after passage of a probe or who had pancreatitis, a bizarre picture was found. The intracholedochal pressures varied: the rate of flow from the duct was decreased and the pain threshold was 10 to 15 centimeters of water pressure.

The value of tests of intracholedochal pressures and volumes have to be carefully scrutinized. Inadequate position of the "T" tube or other technical errors were obvious as a rapid loss of fluid around the tube, or as a varying

character to the discomfort produced by injected fluid, or by a markedly irregular response to the injected fluid. In the course of this investigation, patients were observed in whom the indwelling "T" tube had been kinked or abnormally placed so that pressure and volume readings could not be obtained accurately. In other cases, other technical errors, such as leakage of bile around the tube or an insufficient external length of "T" tube prohibited accurate measurements.

It must be determined that measurements were actually being taken of the fluid content of the common bile duct. It must be known that there was no leakage through or around the "T" tube or that the tube was not kinked. It must then be decided that the fluid filled the common bile duct and/or the hepatic radicles to capacity. If the enlarged radicles are filled prior to the opening of the sphincter of Oddi, there would be greater capacity of the duct. This was particularly true in cases of long standing calculous obstruction to the common bile duct wherein the papilla of Vater has an altered threshhold for relaxation[2,5].

When all these factors had been evaluated, it was necessary to be extremely careful about the position of the zero point level in taking pressure readings. The zero level must be placed at the mid-point in the sagittal plane of the body to be at the approximate level of the common bile duct.

An evaluation of pain reactions must be made in regard to the distensibility of the common bile and hepatic duct walls as compared to the reaction of irritation presented at the sphincter of Oddi and to abnormal positioning of the "T" tube within the duct.

Our results have shown that it was possible to determine physiological attributes of the common bile duct through a careful study of the pressure and volume studies postoperatively through the indwelling "T" tube. This type of study may be repeated frequently without any inconvenience to the patient.

Summary and Conclusion

1. Intracholedochal pressure and volume changes were found to be a direct function of the termination of the common bile duct and its contents.

2. Technical errors such as related to the length of the intraductal "T" tube, leakage around it, the kinking of the "T" tube, partial dedection of the duct, and abnormal collections of fluid or gas may affect the intracholedochal pressure and volume.

3. Abnormalities at the termination of the common bile duct such as traumatic edema, redundant mucosal folds, calculi or spasm may produce enlargement of the duct, an increased intracholedochal pressure, a delay in emptying rate of the duct and significant defects visible on the cholangiogram.

4. Clinical trial by clamping the external limb of the "T" tube, the use of cholangiograms, and the measurements of intracholedochal pressures and vol-

umes all have certain inherent errors. It is hence concluded that all these methods should agree in the individual patient in order to afford most efficient management.

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BENIGN GASTRIC ULCER IN THE PRESENCE OF APPARENT HISTAMINE RESISTANT ACHLORHYDRIA*†

Report of a Case

THOMAS C. WILKINSON, M.D.**
Pittsburgh, Pa.
and
SAUL FORTUNOFF, M.D.‡
Beckley, W. Va.

Gastric ulcer is not ordinarily associated with the high levels of free hydrochloric acid found in patients with duodenal ulcer. In fact, gastric ulcers frequently exist in the presence of normal or low acid levels. Nevertheless, it is our feeling that the old axiom, "No acid, no ulcer", is still valid. To quote from Kirsner, et al[1] "The role of the acid may be likened to that of the indispensable catalyst; its presence facilitates the process of ulceration; its sustained elimination will result in complete and sustained healing, regardless of other factors". In support of this, they report cases of long standing gastric ulcer which healed promptly with the onset of achlorhydria, either as the result of x-ray therapy or of advanced age. These authors, in the same paper, state that it is not the absolute degree of acidity which is important but the relationship of this degree of acidity to the degree of lowered "tissue resistance" of the gastric mucosa.

Nevertheless, cases are occasionally reported in which a benign gastric ulcer is present in a patient who is achlorhydric[2,3]. We feel that the achlorhydria in these cases is only apparent, not real, or perhaps that the achlorhydria is a temporary one and that, if sufficient stimulation is used in a large enough number of tests, the presence of free hydrochloric acid can be demonstrated in all cases.

Shay and his associates[4] have stated that, while Topfer's reagent is adequate for determining levels of free hydrochloric acid clinically, a true achlorhydria cannot be presumed from failure of this reagent to change color. They believe that anacidity can be considered to be complete only if the pH of the gastric sample remains at or above the pH of gastric mucus (8.3). They state that complete anacidity can only be assumed if, after adequate histamine stimulation, there is no lowering in the pH of the gastric content. Any drop in the pH of the fractional gastric sample would indicate the presence of acid and would be sufficient indication that some parietal cell function still remains.

*From the Medical Service, VA Hospital, Butler, Pa.
†Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
**Attending Gastroenterologist, Veterans Administration Hospital, Butler, Pa.
‡Chief, Medical Service, Veterans Administration Hospital.

Furthermore, as reported by Levin et al[5], patients with benign gastric ulcer may show a temporary achlorhydria which, on subsequent examinations, becomes positive for free HCl. They conclude that histamine response may be found to be variable from day to day in patients with benign gastric ulcer. Patients receiving x-rays to the fundus of the stomach may achieve a profound depression of the parietal cell function to such an extent that the standard histamine test fails to evoke an acid response. In one such case, intravenous administration of histamine was required to demonstrate that the stomach was capable of secreting free HCl. In another case alcohol by mouth, in addition to intravenous histamine, was required to demonstrate the secretion of free acid.

Greenspan et al[3], report a case of "gastric ulcer with a true anacidity". Their studies for free HCl, however, only cover a period of two months, and one wonders if subsequent follow-up studies would not have shown this to be a case of only temporary anacidity. It is our contention that patients with benign gastric ulcer are sometimes reported as achlorhydric on the basis of too few tests.

Hunt[6], advances the hypothesis that vascularity of the gastric mucosa may control the reactivity of these parietal cells by histamine stimulation. This suggests that the achlorhydria found in older people may be on the basis of atrophic gastritis with poor gastric vascularity and decreased number of parietal cells.

We suggest that the temporary achlorhydria of benign gastric ulcer may be on the basis of: (1) Temporary reduction in the number of functioning parietal cells; (2) Insufficient stimulation of gastric mucosa by means of histamine alone.

We report the following case of a patient with gastric ulcer and histamine resistant achlorhydria in which we proved, quite by accident, that the achlorhydria was only apparent and not real.

Report of Case

A 60-year old white male was admitted to the Veterans Administration Hospital, Butler, Pa., because of a multiplicity of symptoms relating to the urinary bladder, liver, colon, and stomach. He took frequent laxatives for "constipation". He did not give symptoms indicative of peptic ulcer, but complained of "gas, heartburn, and spells of acid stomach condition". The patient manifested great anxiety in the admission office, and he was given an admission diagnosis of gastric neurosis and admitted to the neuropsychiatric service. The first findings on examination were not remarkable, and routine serological tests for syphilis were negative. Chest x-ray was also negative.

On September 7, 1949, a gastric analysis with histamine stimulation was done. This showed complete absence of free HCl. X-ray examination on September 2, 1949, was reported as showing: "gastric ulcer along the posterior wall near the lesser curvature just below the fundus". Gastroscopic examination was done on September 16, 1949. At this time the fasting gastric residue was negative for

free HCl. On the lesser curvature of the stomach a typical benign gastric ulcer was seen and in addition, changes characteristic of chronic hypertrophic gastritis were observed on the anterior wall. The observation was made that these findings were inconsistent with a true achlorhydria. It was recommended that the gastric analysis be repeated and, if achlorhydria was again present, surgical exploration be done. This was suggested because of the possibility that the changes which had been interpreted as hypertrophic gastritis might, in fact, be an early infiltrating carcinoma.

Gastric analysis was repeated on September 19, 1949, with histamine and again free HCl was completely absent. At the request of the Surgical Service it was decided to do another gastroscopic examination before surgical exploration. This was done on September 27, 1949. At this time when the *fasting* gastric residue was tested qualitatively with Topfer's Reagent, free HCl was found to be present. The specimen was sent to the laboratory and was reported to contain 27 units of free HCl. The observation was made that "in spite of prolonged search in the upper portion of the stomach, the ulcer previously described could not be seen". X-ray examination on September 30, 1949, was reported as showing "no definite evidence of the previously noted ulcer. The appearance suggests improvement, if not actual disappearance, of the ulcer."

The patient was discharged from the hospital, symptom-free, on October 28, 1949, with instructions to return in three months for a check-up. He reported back to the hospital on January 5, 1950. During this admission x-ray studies again failed to reveal the presence of a gastric ulcer, and gastric analysis with histamine showed the presence of free HCl in the gastric content with a high point of 20 units in the specimen taken at 45 minutes. It was not felt necessary to perform a gastroscopic examination at this time. During the interval between hospital admissions the patient reported that his weight had increased from 135 pounds to 142 pounds and that he had remained symptom-free.

In May, 1951, almost 2 years after his hospital admission, we received a letter from this patient stating that his weight had increased to 162 pounds, a total gain of 27 pounds; that he was working regularly and had "never felt better in his life".

We feel that this man's continued survival in good health and his sustained gain in weight in addition to the prompt and complete healing of the ulcer adequately prove that we were not dealing with a malignant ulcer.

Conclusions

1. Benign gastric ulcer can and does occur in the presence of apparent histamine resistant achlorhydria.

2. A case is presented in which this achlorhydria was proven to be only apparent.

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INVAGINATION OF THE PYLORUS INTO THE BASE OF THE DUODENAL BULB CAUSED BY SCIRRHOUS CARCINOMA OF THE STOMACH

MAURICE FELDMAN, M.D.

and

PHILIP MYERS, M.D.

Baltimore, Md.

In this report an effort is made to contribute to our further knowledge on protrusions of the stomach into the base of the duodenal bulb. In recent years there has been an increasing interest in deformities involving the base of the duodenal bulb produced by prolapse of the gastric mucosa and invaginations. In a perusal of the literature there has been no case report of invagination at the pyloroduodenal outlet resulting from carcinoma of the stomach.

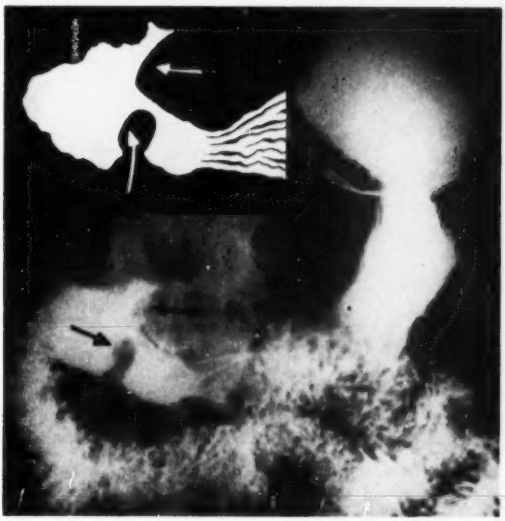

Fig. 1—Roentgenogram made in the prone position illustrates the linitis plastica type of scirrhous carcinoma of the stomach. The invagination of the pylorus producing a filling defect in the base of the duodenal bulb is shown at arrows.

Recently we observed a case of scirrhous carcinoma of the stomach which presented a roentgenogram simulating prolapse of the gastric mucosa or a hypertrophic pyloric stenosis protruding into the base of the bulb. Since there has not been any similar case reported on invagination of the pylorus into the duodenal bulb as a result of carcinoma, we thought it might be of interest to present the following case.

Case Report

Male patient, age 68, complained for three weeks of epigastric discomfort, gas, fullness, belching, poor appetite, feeling worse after eating, nausea, vomiting and some loss of weight. The stools were not black at any time and no visible blood was observed by the patient, but on examination there was repeated evidence of occult blood. On physical examination a sausage shaped hard mass was palpated in the epigastrium. A gastrointestinal roentgenologic study revealed an extensive filling defect involving the entire stomach which was attributable to carcinoma. The stomach was narrowed and tubular. The pylorus

Fig. 2—Right oblique view of the stomach illustrates the narrowing of the pylorus and presents an annular cuff-like defect. The pylorus is invaginated into the base of the duodenal bulb. The crescent-shaped defect shown at the arrows is seen more clearly in this position.

showed an annular cuff-like narrowing which protruded into the base of the duodenal bulb. The contour of the duodenal bulb was otherwise regular, with the exception of the base which showed a smooth crescent shaped deformity. There was a trace of barium retained in the stomach at the end of five hours. The striking feature was the unusual roentgenographic finding of a protrusion of the pylorus into the base of the duodenal bulb. The roentgenogram resembled a prolapse of the gastric mucosa or a hypertrophic pyloric stenosis invaginated into the base of the bulb. At operation there was evidence of extensive involve-

ment of the stomach with a linitis plastica type of carcinoma. On palpating the stomach it was felt to be cartilaginous and rigid. There was considerable annular narrowing of the pylorus at the duodenal juncture. The narrowed pylorus was seen to protrude into the base of the duodenal bulb. The surgical findings confirmed the roentgenologic observation of the invagination.

Comment

This paper is primarily concerned with the unusual roentgenograph of a slight invagination of the pylorus into the base of the duodenal bulb as a result of a scirrhous carcinoma (linitis plastica) of the stomach. As far as can be ascertained, the invagination resulting from this condition is apparently a new roentgenologic sign which has not been reported previously. We have never observed this sign in other forms of carcinoma excepting the linitis plastica or scirrhous form involving the pylorus. It must be emphasized, however, that the invagination of the pylorus into the duodenal bulb is not always present in this condition. It is noteworthy to point out that simulating roentgenographic results may be seen in other conditions, namely, (1) prolapse of the gastric mucosa into the duodenal bulb, (2) prolapse of a gastric polyp into the base of the duodenal bulb, (3) hypertrophic pyloric stenosis invaginating into the base of the bulb, and (4) invagination from other causes, such as those resulting from neoplasms.

Summary

Invagination of the pylorus into the duodenal bulb may produce a roentgenologic picture simulating several conditions. In a review of the available literature there has not been a case report of invagination of the pylorus into the duodenal bulb produced by scirrhous carcinoma (linitis plastica) of the stomach. This roentgenologic finding seems to be a new sign for this condition. A case of scirrhous carcinoma of the stomach with surgical confirmation of invagination of the pylorus into the base of the duodenal bulb with roentgenologic findings is reported.

ANTIRETENTIONAL MIGRAINE THERAPY*

EUGENE FOLDES, M.D.†

New York, N. Y.

Always, in a scientific discussion, it is useful to employ clearly defined terms. For this reason I should like to state what is meant by the terms "antiretentional", "migraine" and "therapy", which make up the title of this presentation.

Examining the term migraine first I am not going to waste your time with details of description but there are a few facts which I believe should be kept in clear focus. These in migraine are the role of heredity, the periodicity of the headaches and their frequent appearance in the form of hemicrania. Significant also are the association of headaches with visual disturbances and with such gastrointestinal symptoms as nausea or vomiting. Chiefly it is the more or less simultaneous manifestation of headaches with gastrointestinal symptoms which may lead to diagnostic difficulties. Impressed by the dramatic occurrence of vomiting, patients sometimes ascribe the headache to upset stomach and, while complaining of the latter, mention the hemicrania only on questioning. They then frequently use the term of "bilious headache". We must not be misled. Of headache caused by upset stomach or gallbladder disease it is necessary to say that there is no such thing. When vomiting and headache occur together they are, almost without exception, coordinated manifestations of changes taking place in the brain.

I hope it will not seem pedantic to discuss the definition of the term "therapy". According to the dictionary therapy is the "department of medical science that treats of remedies for disease". In this connection we are often confronted by the question as to whether a remedy, which is felt by the individual patient to be worse than the disease, still comes under the heading of therapy. On this problem I shall have more to say later.

Trying to define the meaning of the third term employed in the title of this presentation we arrive at the basic issue. Almost twenty years ago I proposed the concept according to which the attack of migraine is caused by retention of liquids in the brain. Thus the aim of therapy should consist of elimination of liquids retained and prevention of their reaccumulation. Hence, the term "antiretentional"[1,5]. The terms diuretic, or dehydration, therapy did not seem adequate not only for reasons of semantics but also for reasons which were eminently practical. In the term "antiretentional" the thought and the warning is expressed that only excess liquids should be eliminated, while the normal fluid content of the body must be safeguarded. The aim is an *euhydric state*[1] of the individual. There is no such implication in the expression, diuretic therapy or dehydration.

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†Adjunct Professor of Gastroenterology, New York Polyclinic Medical School and Hospital.

The practical significance of this is that applying diuretic or dehydration methods carelessly the delicate water and electrolyte balance of the organism may be upset with harmful consequences.

Water Metabolism in Migraine

Returning now to the proposition that in the pathogenesis of migraine intracranial liquid retention, or in other words swelling of the brain, is a significant factor, this concept suggested itself through the following reasoning[1-3].

Aside from migraine, paroxysms of headache, vomiting and visual disturbances also are seen in uremia. In uremia there seems to be little doubt that it is the accumulation of fluids in the brain tissue and within the cavities of the brain which leads to the aforementioned triad and also to convulsions. Since the symptom-complex of headaches, vomiting and visual disturbances is the most characteristic finding in migraine the question arises whether the similarities are merely casual or are due to the working of the same factors in both instances. The question can be formulated in yet another manner, i.e. whether migraine is caused by intracranial accumulation of liquids and whether this in turn is produced by general retentions. It seems that this question can be answered in the affirmative. Because of lack of time I am going to omit mentioning the many examples which can be quoted to illustrate the point and will refer to my publications[1,2].

What happens to liquids retained during the attack? They are eliminated at the end of the migraine paroxysm. I called attention to the fact that the long-known "urina spastica" can be interpreted in this sense[1,2].

The results of these investigations were substantiated during the course of the years. Out of the many such reports I shall here only mention Campbell's observations[6] with reference to generalized retentions and Goltman's contribution[7] as to the presence of edema in the brain in the migraine attack.

Campbell and her associates find that the blood sodium level is high in the prodromal phase and further increases during the attack. The blood sodium returns to normal in recovery and remains normal in the interim phase between attacks. It was also observed that the total proteins of the blood are below normal both before and during an attack and rise again to normal values in the interim. Campbell interprets these findings as signs of overhydration in the blood throughout an attack of migraine.

Regarding the presence of swelling of the brain Goltman described a case of migraine in which craniocerebral exploration during attack revealed a tense nonpulsating dura, a wet brain and fluids which were under increased pressure. The patient was observed for some time after the operation and it was noted that the opening of the skull bulged out as an attack progressed, indicating edema of the brain. At the termination of the attack the swelling gradually receded.

Origin of Disturbed Water Metabolism in Migraine

If it is accepted that there is a water retention in migraine and that this is the direct cause of the attack the question as to the origin of the disturbed water metabolism should be examined. I here found partly intrinsic and partly extrinsic factors[1,2]. Among the intrinsic factors the sex hormones should be mentioned first. The hormones produced by the ovaries promote retention of liquids and I called attention to the fact that this occurrence explains the phenomenon that in women, before and during menstruation, when the hormonal discharge is increased, the frequency of migraine attacks is greatest. It should be mentioned that the male sex hormone also promotes liquid retention. I pointed out that other endocrine organs may also play a part in the disturbances of water metabolism leading to migraine and mentioned chiefly the antidiuretic hormone of the posterior lobe of the pituitary. To these may now be added the various adrenal cortical hormones.

Among the extrinsic factors which may lead to water retention and thus to migraine, the diet is the most important. It is a well established fact that protein-poor diet my lead to the development of edema, and conversely increased protein intake leads to increased diuresis. The effect of a diet, rich in carbohydrates, on the water metabolism is opposite to that of protein-rich diet inasmuch as a carbohydrate-rich diet results in water retention. A fat-rich diet similarly leads to water retention. Vitamin deficiencies are in general associated with retentions of liquids. These liquids are eliminated when the deficiency is corrected so that at least to this extent vitamins have antiretentional action.

As to the effect of increased water intake on the state of hydration of the body, it seems that under certain circumstances there may be retention while under others increased elimination may occur. Restriction of the water intake leads to decreased hydration of the body. When a certain amount of sodium chloride is administered without additional water it may be entirely eliminated, usually with considerable water diuresis. A salt-poor diet is followed by losses in the sodium and water content of the body. Upon the simultaneous introduction of large quantities of both water and sodium chloride, retentions usually develop.

It can be seen that in patients suffering from migraine, a diet poor in proteins but rich in carbohydrates, fats, water and sodium chloride may lead to retentions and thus development of an attack.

At this point the question should be examined as to why, in the presence of generalized liquid retention in migraine, local accumulation takes place in the brain rather than in some other organ. In several publications I proposed[1-5,8,9] that for the development, not alone of migraine, but also of certain other diseases such as angina pectoris, Ménière's syndrome, etc., two factors are necessary. The one is a disturbed general water and electrolyte metabolism while the other factor is a local predisposition for temporary accumulation of liquid in one organ or

another. I suggested that the local predisposition is the result of local circulatory disturbances. We may identify vasoconstriction and vasodilation, which are so much emphasized in the pathogenesis of migraine today, as these local circulatory disturbances. Because in migraine they are located in the brain rather than in another organ, such as e.g., the myocardium, the labyrinth of the ear, etc., headache rather than angina pectoris, Ménière's syndrome, etc., will develop.

Therapy of Migraine

From what has been said it follows that if we aim at more than a symptomatic therapy of migraine our goal should be elimination of retained liquid and prevention of subsequent liquid accumulation. For this purpose I suggested a diet[1-5] which is rich in foods having antiretentional action such as proteins and vitamins and is restricted to a greater or smaller extent in carbohydrates, fats, liquids and sodium chloride all of which are conducive to liquid retention. In twenty-four hours this diet contains approximately 1.5 gm. of proteins and 2.5 gm. of carbohydrates per kg. of ideal weight and from 40 gm. to 50 gm. of fats.

For a male patient of average height a diet would be given which would contain daily approximately 115 gm. of protein 200 gm. of carbohydrates. 40 gm. or 50 gm. of fats, the vitamins in their natural sources, only moderate amount of table salt and six glasses of liquids, including one glass of fruit juice and one cup of coffee.

The therapeutic results which can be obtained by this diet in migraine are excellent in the majority of cases good in others but hardly ever completely absent[1,2]. The results were confirmed.

Nevertheless, it became desirable to find an alternate method of treatment mainly because of two sets of circumstances which interfered with the successful application of the dietetic therapy. The one is inherent in all treatments with diets and is caused by the difficulty most patients experience in observing restrictions for protracted or even indefinite periods. There are patients by whom all restrictions, dietary or otherwise, are felt and resented as intrusions into their personal freedom and are abandoned gradually in spite of the improvement which they experience and even if, when making up the diet within its general framework, consideration is given to individual preferences and dislikes. To these patients the remedy is worse than the disease, an occurrence to which I referred in the introductory remarks to this presentation. Application of therapeutic measures other than dietetic was necessary also in cases in which migraine occurred together with diseases which called for a diet contrary in certain features to those applied in the antiretentional therapy, as for instance, in the not infrequent combination of migraine with peptic ulcer. In the latter the administration of frequent feedings consisting chiefly of starchy foods and a liquid (milk) is incompatible with the low carbohydrate and restricted liquid intake of the migraine diet.

For these reasons a trial with diuretics was decided upon. The therapeutic effects of mercuhydrin, aminophylline and of the combination of the two were observed[5]. Mercuhydrin was injected intramuscularly once weekly in the dose of 1 c.c. This relatively small dosage was selected in view of the antiretentional rather than dehydrating aims of our therapy. Aminophylline was given either orally in doses of from 0.1 gm. to 0.2 gm. three times daily or in the form of rectal suppositories at night or every other night in the dose of 0.5 gm.

Therapeutic results were observed in all cases from mercuhydrin as well as from oral or rectal aminophylline or from the combined administration of the two drugs. Improvement was noted in the frequency, the severity and the duration of the migraine attack. Therapeutic response was manifest in most cases almost immediately but it usually did not reach its peak before two or three months of therapy.

As to the selection of the form of therapy in the individual case as to whether mercuhydrin, aminophylline or a combination of the two should be employed we may be guided by the following principles. Injection of mercuhydrin should be applied if oral or rectal aminophylline is to be avoided because of local irritation in the stomach or in the rectum. Mercuhydrin injection therapy also recommends itself by its elegance and by a minimum of undesired side-effects. If administration of injections meets with difficulty, oral or rectal aminophylline may be given. Finally, combined therapy may be employed if quick and complete results are desired and if aminophylline is well tolerated.

It is noteworthy that the remission does not end with the cessation of active therapy but usually lasts for periods of from several months to more than a year. The best results, not only as to the length of remission but also as to the extent of improvement, were obtained in cases in which the treatment was continued for three months or longer. This would seem to show that the elimination of retained liquids may require, in migraine, a period of months and similarly that it may take a period of months before reaccumulation of liquids reaches a level at which the clinical symptoms of migraine again become manifest. I observed that the resumption of active therapy at the time of relapse is followed by renewed improvement so that one can hope that, with treatments repeated periodically, sufferers from migraine can be kept in a state of remission for indefinite periods.

Summary

The migraine attack is produced by a swelling of the brain in the presence of general liquid retention.

The migraine attack can be prevented to an extent which is therapeutically significant by elimination of retained liquids and prevention of their subsequent accumulation. This aim can be accomplished by the antiretentional diet. It can

also be accomplished by the administration of mercuhydrin, aminophylline or the combination of the two.

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A CASE OF GUMMA OF LIVER DIAGNOSED BY LIVER BIOPSY

VIKIT VIRANUVATTI, M.D., M.P.H.*

and

SUED KOCHASENI, M.D.

Bangkok, Thailand†

Liver biopsy has been done in the Department of Medicine, Siriraj Hospital, University of Medical Science since 1950 as an adjunct in the diagnosis of obscure cases of liver diseases; in the study of systemic disease as well as for differentiation between intra- and extrahepatic jaundice. In our experience with thirty-three biopsies there has been no fatality or serious complication. Gallison and Skimmer (1950) collected case reports from 1923 to July 1950 and found a total of 4,911 cases of liver biopsies and more recently, Cassel et al (1951) mentioned that there had been around 5,000 biopsies done with seventeen mortalities. There has, however, been no report on the findings of gumma of liver diagnosed by liver biopsy, thus we think it that it is worthwhile to publish this case report.

Case Report

A 36 years old Thai female U.N. 23968.94, A.N. 6142.94 was admitted to the Medical Department, Siriraj Hospital, Bangkok, Thailand on June 11, 1951 with the chief complaint of pain in the right hypochondrium for 15 days. The present illness began about a month prior to admission when she began to notice a painless swelling in the epigastrium. The mass gradually enlarged downwards with subsequent development of pain and tenderness. Pain was dull aching, intermittent in character without relation to food. Three days prior to admission she developed fever and chills with pain on the mass aggravated by respiration and she had to lie flat in bed. During this period the patient was anorexic and dull. Bowel movement was always normal.

Past history revealed amebic liver abscess seven years ago and was admitted in this hospital and discharged as cured case, typhoid and malaria several years ago.

Physical examination revealed thin, emaciated, weak without edema, cyanosis or jaundice. No telangiectatic spots were seen. T=37.9° C. P=80/min. R=22/min. B.P. 122/90 lt. arm. Body weight on admission=35 Kg.

Alimentary system: teeth, tongue and tonsils normal.

*Instructor in Gastroenterology and Tropical Medicine, Siriraj Hospital, University of Medical Science.

†Instructor in Medicine, Siriraj Hospital.

Abdomen—liver, enlarged especially left lobe about five finger breadths under xiphoid cartilage and bulged out as a semiglobular swelling in the epigastrium, it was firm with rather smooth surface and moved with respiration. Slight tenderness was elicited on deep pressure. No superficial dilated veins and ascites. Spleen was not palpable.

Respiratory system—Chest movement was normal, no adventitious sounds were audible.

Cardiovascular system—Heart normal size, no murmurs.

Lymphatic system—No enlarged superficial lymph glands.

Other systems were noncontributory.

Laboratory Findings:—

Blood	June 12	June 13	July 17	Aug. 10	Sept. 13	Oct. 16
Hb.	54%	52%	50%	55%	55%	40%
R.B.C.	3.8 m.	4.2 m.	3.79 m.	3.3 m.	4.33 m.	—
W.B.C.	6400	6600	5050	5050	6500	5400
Poly.	90%	86%	65%	60%	65%	72%
Lymph.	10%	14%	28%	35%	33%	26%
Eos.	—	—	5%	—	2%	2%
Baso.	—	—	—	—	—	—
Mono.	—	—	2%	—	—	—

June 16. Blood cholesterol 108.1 mg % Blood group O Landsteiner. Blood Kahn 4 +.

June 13. Serum albumin 4.7%, globulin 3.1%. Blood Creatinine 1.6, N.P.N. 22.7, Urea 40.4 mg %.

August 9. Serum albumin 4.2%, globulin 2.6 %. Blood Creatinine 1.2, N.P.N. 25.4, Urea 38.6 mg %.

Malaria negative on seven occasions.

Urine—normal. Feces—positive for Ascaris lumbricoides ova.

Fluoroscopy June 20: Fluoroscopy showed normal heart and lungs. Right dome of diaphragm showed very slight relatively limited excursions.

G.I. Series: Esophagus appeared normal. Stomach was medium in size, low in position, displaced downwards and slightly displaced to the left, showing fairly smooth good tone, outline and normal peristalsis. There was no residue at the end of six hours. Duodenal cap was medium in size, well filled and being displaced downwards. Motility was average, the head of barium column being in hepatic flexure of colon after six hours. Cecum and hepatic flexure of colon appeared well filled, free and not tender. The hepatic flexure of colon appeared in normal position. Impression: Extragastric mass.

Provisional Diagnosis. Hepatoma, Ascariasis, Syphilis, latent.

During the period of admission the patient ran a low grade fever around 37.8° C. in the afternoon. The agglutination for typhoid and paratyphoid were done and showed negative results. Bromsulfalein excretion test showed complete clearing of the dye from the serum within 30 and 45 minutes.

With regard to the findings of globular swelling of the liver, firmness, debilitated condition of the patient weighing only 35 Kg. on admission with development of symptoms within the period of three months the probability of malignant neoplasm of liver was considered. With reference to nonicteric condition of the patient, the primary liver cell carcinoma or hepatoma was given as provisional diagnosis. As we ran short of materials for determination of a battery of liver function tests, liver biopsy by subcostal approach was performed by puncturing the needle directly on the mass on August 29, 1951 obtaining the following results from the Department of Pathology: "No definite liver tissue is present. Area of necrosis and giant cells can be seen, suggestive of gumma or malignant growth. Rebiopsy should be done."

Rebiopsy was performed on November 9, 1951 by the same method and approach obtaining the following microscopic findings: Liver cells show irregular shape, size and arrangement. There is a slight amount of fibrosis which is irregularly distributed. There are no bile duct thrombi. There is apparent proliferation of bile ducts. Diagnosis: Liver, fibrosis.

Progress:—As the result of four plus blood Kahn, Bismuth salicylate was given intramuscularly totalling 1.4 gm. and later Procaine Penicillin G. in oil and beeswax suspension 600,000 O.U. daily totalling six million units. The patient became afebrile on the seventh week. During this period she regained her appetite and vitality and gradually gained weight to the maximum of forty-one Kg. after four months of hospitalization. Pain gradually decreased and became absent, she was then up and around. Before discharge the liver reduced in size to about three fingerbreadth under xiphoid cartilage, lost its bulging contour, and became painless. Finally she was discharged on November 14, 1951. Symptomatic treatment including crude liver extracts were given during the period of hospitalization.

Comment:—Syphilis is a prevalent disease in our country and cases without adequate treatment are common so we have a rather fair chance to have cases of gumma of liver. In this case, the result of the first biopsy showed areas of necrosis and giant cells suggestive of gumma of liver of malignant growth. The latter may be ruled out easily by the clinical improvement after antileutic measures, the progressive gain in weight of 7 Kg. during admission, reduction in size of the liver itself and the improvement of general condition of the patient. The second biopsy result was obtained after treatment and found only fibrosis of the liver which fit in with the resultant finding of liver necrosis.

Conclusions

1. A case of gumma of liver diagnosed by liver biopsy together with beneficial clinical result after treatment with antileutic measures is reported.

2. The correlation with the biopsy result and clinical findings is very important in the diagnosis of obscure liver disease.

We would like to express our sincere appreciation to Dr. Prasert Kangsdalya, head of the Department of Medicine, for his guidance, enthusiasm and willingness, Dr. Frank Vellios, Dr. Sangad Kanjanakunchorn of the Department of Pathology, for their effort and sincere cooperation in preparation and reading microscopical sections. Without their efforts, the preparation of this manuscript would not have been possible.

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SOME INTERESTING EXPERIENCES WITH JAUNDICE*

JACOB A. RIESE, M.D.
West New York, N. J.

Jaundice most frequently presents an experience in mental arithmetic from which one can come up with the right answer. Occasionally, however, one arrives at a questionable conclusion. Such a case is this one of a 40 year old female who came to my office complaining of diarrhea recurring for six months. Diarrhea was associated with cramp-like pains in the upper right quadrant, and considerable gas by rectum and by mouth. Stools contained mucus and a small amount of blood. A check-up in a hospital two months previous to her first appearance at my office was completely negative. Her previous history consisted of a hysterectomy and an operation for a fractured elbow one year earlier. No transfusions were given for these hospital admissions.

At my office x-rays of the colon, and sigmoidoscopic examination revealed no pathology. X-ray examination of the chest and gallbladder were negative. Stomach and small intestinal tract were normal. Physical examination revealed no abnormalities. Gastric analysis was normal, but duodenal drainage and stool examination disclosed the presence of Giardia lamblia. No occult blood was present in the stool. Stool cultures were negative for typhoid and paratyphoid organisms. Because of the completely negative findings other than the presence of Giardia lamblia I concluded that the latter findings were responsible for the recurrent attacks of diarrhea.

Specific treatment for Giardia lamblia was given in the form of atabrine 1½ grains four times a day. Patient was warned that she would get a yellowish discoloration of her skin. She did get it, but as I continued to observe her, the yellow discoloration gradually changed to a deep jaundice. Atabrine had been given for ten days. She was now admitted to the hospital. On admission she had a smooth palpable liver edge five centimeters below the costal margin. She was deeply icteric, her temperature ranged between 99.6° and 100.6°; she had a pulse rate of 90. The white blood count on admission was 1,850 with 74 lymphs; 2 polys; 2 segmented forms and 5 stabs; 15 eosinophiles and 2 basophiles. Serum bilirubin was 13 milligrams; total cholesterol was 427; cholesterol esters were 219 and she had no urobilinogen in her urine. Stools were clay colored. There was bile in the urine. Two weeks after admission, serum bilirubin had gone up to 22; her prothrombin was 50 per cent of normal. There was four plus occasional occult blood in the stool. Three weeks after admission a liver biopsy showed biliary stasis; an alkaline phosphatase of 23 and cephalin flocculation was negative. Other studies done at this time revealed bleeding 2½ minutes; clotting time 4½ minutes; a negative Wassermann and her blood was negative for heterophile

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antigens. Four days after admission a re-check of blood picture showed a rise in white count to 7,400 with 64 per cent segmented form; 30 per cent lymphs; 3 per cent eosinophiles and 3 stab forms.

One month after admission we decided to operate. At operation the hepatics were small and empty; the common duct was small and collapsed; the gallbladder was collapsed and empty; no glands were found. A "T" tube was placed in the common duct; pancreas was normal and the pancreatic ampulla was normal. A cholangiogram was done three weeks after operation and x-ray studies were completely negative. Four weeks after operation urinary urobilinogen was not present; the white blood count had returned to normal; the liver was still enlarged and jaundice was still present. Patient was discharged from the hospital 2½ months after admission with an enlarged liver and a marked jaundice. The patient's jaundice continued, sometimes becoming a little lighter and sometimes deepening. Ten months after onset of jaundice the patient still had an enlarged liver and was still jaundiced. At that time aureomycin had recently been introduced, so we tried aureomycin and the patient appeared to improve for two weeks after its administration. Because of her continued improvement we kept her on large amounts of aureomycin, from which she then developed a toxic reaction. One year and two months after the onset of jaundice she had recovered substantially, but there still was a tendency to the occasional recurrence of slight icterus; a palpable liver edge two inches below the costal margin persisted. Liver enlargement and jaundice had completely disappeared by the end of the second year of her disease.

The foregoing problem resolves itself into three possibilities: (1) atabrine toxicity; (2) obstruction of the cholangioles by Giardia as a result of the chemotherapeutic effect of atabrine; (3) cholangiolytic jaundice on a virus basis. We have not been able to find any literature on liver toxicity due to atabrine despite the millions of doses of the drug used in the Army. The diagnosis of cholangiolytic obstructive jaundice is a diagnosis made by default when nothing else explains the obstruction. On the other hand Giardia lamblia infests the duodenum and biliary tract and it is conceivable for these small organisms to have instigated the obstructive signs. Rubin claims to have seen such a case.

Sometimes one can fall into a mistaken diagnosis if one jumps at the obvious. L. R. is a 65 year old male whom I have had under my observation for 20 years. He has a large solitary gallstone which was discovered by accident and which has never given rise to any symptoms. One day this patient walked into the office with a deep icterus and an enlarged liver. He had just been advised by his family physician to have his gallbladder removed because of complications which had arisen due to the presence of gallbladder pathology with stones. A complete history elicited a blood transfusion some two months previously. A Liver Battery disclosed hepatocellular damage. This patient was treated conservatively for a presumptive diagnosis of serum hepatitis. All findings cleared completely in three weeks and the patient has been well now for three years.

This case is representative of a number of such cases that I have seen. Since the mortality rates are quite high in operative procedure in the presence of hepatitis—it is important not to fall into the trap of the obvious diagnosis.

In this modern day of the virus it is well to remember that an old fashioned bacterial infection can cause jaundice. A 33 year old male developed a salmonella infection after eating raw clams. Jaundice with enlargement of the liver and diffuse hepatocellular damage occurred. After eight weeks of medical care jaundice disappeared, liver receded to normal and patient has been entirely well. Paratyphoid infection is frequently associated with the eating of shell-fish. An ascending biliary tract infection from the gallbladder is thought to be the cause of jaundice in these cases.

Jaundice can be a complicated unanswerable problem as in the first instance, or it may resolve itself after careful study into an interesting experience in diagnosis.

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REDUNDANT SIGMOID SIMULATING HIRCHSPRUNG'S DISEASE

BERNARD J. FICARRA, M.D.

Brooklyn, N. Y.

The usual definition of congenital megacolon, or Hirschsprung's disease, is a hypertrophy and dilatation of the colon without mechanical obstruction. In this limited group of individuals with congenital megacolon the pathogenesis of this condition has been the subject of much debate.

Most of the evidence advanced corroborates the thought that the disease is congenital in origin. Recent information suggests that neurogenic deficiency within the bowel itself may be the initiating factor[1,2]. It is not the purpose of this report to discuss the etiologic concepts, but rather to present a case study of a young patient with a redundant sigmoid that simulated congenital megacolon clinically and roentgenologically.

Fig. 1 Fig. 2 Fig. 3

Figs. 1, 2 and 3—Three different views of the lower bowel following barium enema showing a degree of dilatation of the lower colon and rectum.

Case Report

M.L., a ten year old girl, has had "bowel trouble" since infancy. Her complaint was one of severe chronic constipation with bouts of obstipation. During the past two years this complaint has become more severe and distressing. Although slightly anemic she showed no evidence of malnutrition.

She would have periods of exacerbation of the disease in which abdominal cramps and nausea would be the chief complaints. The most significant physical finding was abdominal distention which varied from time to time. During an exacerbation, with the patient standing in an erect position, the dilated bowel could be seen distending the abdomen. It gave the impression that the child

was pregnant. Barium studies of the lower bowel (Figs. 1, 2 and 3) showed a marked degree of dilatation of the lower colon and rectum.

The patient was prepared for surgery with the preoperative diagnosis of Hirschsprung's disease. Laparotomy revealed a markedly redundant sigmoid of normal caliber. Large fecal impactions were outlined. Despite these impactions in the colon, rectal examination demonstrated an empty ampulla. This was in keeping with the original descriptions of megacolon[3].

No resection of the bowel was performed. Plication and shortening of the sigmoidal mesentery was accomplished. The sigmoid was sutured to the lateral peritoneum. These procedures were performed as a prophylactic measure against a future volvulus. The appendix was removed. The patient had no postoperative complication. She now follows a bowel hygiene regimen to combat constipation. This medical procedure has been beneficial thus far.

Discussion

This patient presented a clinical picture strongly suggestive of congenital megacolon. The x-ray studies led credence to the possible presence of Hirschsprung's disease. The roentgenologist is a valuable consultant in evaluating this disease. Patients suspected of having a megacolon should have a fluoroscopic examination of the colon during the administration of a barium enema. Functional obstruction by a dyskinesia of the rectum or rectosigmoid can be detected when the barium mixture is allowed to enter the rectum slowly in small quantities. Satisfactory visualization of the rectosigmoid is accomplished best when the patient is examined in the oblique position. If there is evacuation of the barium by peristaltic expulsion, and if there is a satisfactory emptying of the colon, then Hirschsprung's disease is not usually present.

Summary

A case study is presented of a ten year old girl who presented a clinical picture suggesting congenital megacolon. At operation the true pathology was found to be a greatly redundant sigmoid.

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SIGNIFICANT FACTORS IN THE ETIOLOGY OF GASTROJEJUNAL ULCER*

MICHAEL W. SHUTKIN, M.D.

Milwaukee, Wisc.

Gastrojejunal, marginal and anastomotic ulcer are terms used synonymously for the postoperative, peptic ulcer occurring at or near the site of the suture line uniting the acid secreting gastric mucosa to the jejunum. It is the most serious and frequent complication of gastric surgery for peptic ulcer, and summarily establishes the failue of this surgery. The contemporary popularity of gastroenterostomy with vagotomy and subtotal gastrectomy, with or without vagotomy, has not adequately resolved this morbid change. The age incidence of gastrojejunal ulcer is usually between 30 and 50 years and as suggested by Gaither[1], probably occurs in 15 to 20 per cent of all operations for nonobstructing duodenal ulcer and less frequently after partial gastrectomy than after gastroenterostomy.

The symptoms and signs of gastrojejunal ulceration are recurrent, intractable pain, hemorrhage that has proved refractory to medical management, roentgenologic evidence of gastrojejunal ulcer, a nonfunctioning gastroenteric stoma. A reactivation of a duodenal ulcer which, when it occurs, is always secondary to a malfunctioning gastroenteric stoma. Walters and Priestley[2] observed that the symptoms of gastrojejunal ulcer, severe enough to require more surgery, developed after a gastroenterostomy in the average of 9.3 years, and after gastric resection in 3.3 years. Skoog-Smith[3] noted a 30 per cent incidence of hemorrhage and Jeffrey[4] a little less than 10 per cent of perforations in jejunal ulcer. Perforation may occur with or without a fistula, and the dreaded complication of gastrojejunocolic fistula is said to occur in 10 to 30 per cent. A positive roentgenologic diagnosis depends upon the demonstration of an ulcer niche or fleck retention, and the analysis of a very recent series[2] disclosed a correct preoperative roentgenologic diagnosis of gastrojejunal ulcer in 67.2 per cent of cases when the transabdominal approach was used. Gastroscopy as a valuable diagnostic adjunct will reveal postoperative gastritis, anastomotic ulceration and dilatation of the afferent or efferent loop. Failure to visualize the crater gastroscopically does not rule out the presence of a marginal ulcer. Stevens and Kipen[5] wrote discouragingly of the enigma in the prevention and treatment of gastrojejunal ulcer, which may be less mysterious after emphasizing significant factors in their development.

The dynamic etiology in gastrojejunal ulcer is also present in gastric and duodenal ulceration; but in the marginal ulcer the acid-pepsin component and the ulcer diathesis have appeared expendable when their role is dominantly indispensable. Infection and gastritis remain unproven etiologic factors, while a faulty gastroenterostomy undoubtedly conditions the tissue to peptic ulcera-

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tion. The alkaline duodenal secretions must bathe the anastomotic jejunum and neutralize the acid gastric chyme or ulcer will follow. For similar reasons, the enteroenterostomy anastomosis, with a long loop gastroenterostomy, has been discarded. Conversely, anastomotic ulcers do not occur in histamine refractory achylia after gastroenterostomy and the usual low acid level in gastric ulcer accounts for the rare anastomotic ulcer after surgery for this disease. Janowitz[6] reported a case because it suggested that factors other than HCl and pepsin were responsible for the chronicity of peptic ulcer. The acid-pepsin factor may be viewed as the spirit of the ulcer diathesis, which requires for definition, marked vagotonic tendencies[7], often a positive family history, grade four hyperchlorhydria, frequent recurrences, and often perforation in spite of good medical management. In this category of ulcer susceptibility, postoperative ulcer may follow any type of anastomotic surgery and may continue having recurrences even after one or more partial gastrectomies. The ulcer diathesis and the acid-pepsin factor require greater attention in the prevention and treatment of gastrojejunal ulcer. The following case report will illustrate this point:

Case 1:—R. W., white, married male, age 30 had a duodenal ulcer at 14, with perforation and closure at 17. Several months postoperatively, ulcer symptoms recurred and remained intractable. At age 28 he submitted to a vagotomy with posterior gastroenterostomy and resection of the duodenal ulcer, and then remained symptom-free for one year when roentgenography revealed a penetrating, jejunal ulcer, secondary to vagotomy and gastroenterostomy. With fractional histamine gastric analysis, the highest level of free HCl was 104°. Operation disclosed a penetrating, jejunal ulcer into the transverse colon down to the mucosa. Six months following a subtotal resection, ulcer-like symptoms recurred.

Comment:—The evident ulcer diathesis and hyperchlorhydria repeatedly resisted medical and surgical therapy in spite of vagotomy and partial resection. Anastomotic surgery offers a grave risk in these patients and requires absolute indications and rigid postoperative medical management, if gastrojejunal ulcer is to be avoided.

The persistence or the recurrence of symptoms following an anastomotic operation for peptic ulcer has many diagnostic implications. A provisional diagnosis of gastrojejunal ulcer can be made on any patient with ulcer-like distress, if a symptom-free period followed an anastomotic operation for duodenal ulcer, in the absence of a postoperative achlorhydria. Diagnosis is possible in nearly all cases through analysis of the history, physical findings, roentgenologic studies, gastroscopy and gastric secretion. Following gastric surgery, every patient should have a roentgenologic study before discharge, as a record of the postoperative anatomy. The following case report emphasizes this necessity and the insidious quality of ulcer diathesis.

Case 2:—D. M., white, married male, 58, reported a family history of ulcer and a duodenal ulcer for 20 years. He has had an incompatible and intolerable

domesticity for 25 years. Six years ago a subtotal gastrectory for a gastric and duodenal ulcer was performed without a roentgen study on discharge. Five years later the ulcer symptom-complex with roentgen motility abnormalities in the gastric segment was observed without a positive diagnosis. Our roentgen studies demonstrated a large stomal ulcer which was treated by infradiaphragmatic vagotomy[2,5,8-11]. After 10 postoperative months in remission, symptoms, signs and x-ray evidence of a gastrojejunal ulcer recurred.

Comment:—Subtotal gastrectomy and a subsequent vagotomy failed to arrest[11,12] recurrent, marginal ulceration in the ulcer diathesis with primary combined gastric and duodenal ulcer. This type of patient should have received a very comprehensive and extensive medical regime before being subjected to an anastomotic operation, and thus avail himself of the best prophylactic program against marginal ulcer. In this instance, as in many others with ulcer disease, the medical management requires a readjustment of the mental-environmental situation responsible, in some measure, for his illness. This improvement between the psyche and the environmental influences will prove of the utmost importance and may be essential to a permanent cure. Hospitalization, vacations, and corrective hygiene may adequately initiate the psychotherapeutic approach, while the well established dietary-drug regime consolidates the convalescence. The surgical mortality and recurrences are high in gastrojejunal ulcer, while medical treatment for this lesion has a selective status by affording a maximum of safety and a limited success.

The postoperative management for gastrojejunal ulcer must sustain this rigid, conservative ulcer regime with the abolition of psychic trauma, tobacco, coffee and alcohol. Marshall[13] advocated a second more radical resection, and not simply a vagotomy, in the patient who developed a jejunal ulcer following inadequate gastric resection, since a properly performed resection offers the best opportunity for relief of symptoms and less chance for the development of another jejunal ulcer. In recurrent ulceration, after repeated resection, total gastrectomy may be necessary. The average length of time in which a jejunal ulcer developed in Marshall's series was 1.58 years, while the shortest interval after operation was one month, and the longest 13 years.

Inadequate gastric resection with vagotomy, long proximal jejunal loop with enteroenterostomy and rapid appearance of a jejunal ulcer, are well illustrated in this case.

Case 3:—P. S., white, married male, 41, reported an ulcer history of 16 years, with severe postprandial diurnal and nocturnal pain relieved by food and alkali. Histamine stimulated gastric fractions contained up to 78° of free HCl. Roentgenologic study disclosed a large, penetrating, postbulbar duodenal ulcer for which a subtotal gastrectomy, with a long afferent loop vagotomy and enteroenterostomy, were performed. Four months later a large, penetrating jejunal ulcer was observed on x-ray.

Comment:—Failure of the advanced duodenal ulcer to respond to an adequate ambulatory medical regime usually benefits from the psychosomatic advantages of hospitalization. Should this ideal management fail to bring about a remission, surgical intervention, followed by a similar postoperative medical regime, is mandatory if the surgical benefit is to remain permanent. The prophylactic surgical management of gastrojejunal ulcer, in this type of hyperchlorhydric diathesis, demands absolute surgical indications, very high subtotal gastrectomy alone or with vagotomy[14], short jejunal loop without an entero-enterostomy and an intense postoperative medical ulcer regime. These principles particularly apply to the problem where perforation of a gastric or duodenal ulcer occurred in the past medical history, for it reflects a similar intractability[15] of the ulcer diathesis as occurs with emotional trauma, and in the perforated walled-off ulcer with or without a neurosis[16].

The undesirable consequence of this case resulted from an under-estimation of the ulcer diathesis, inadequate bed confined medical therapy and unphysiologic surgical technic. These are significant factors in the ulcer problem.

The prognosis of marginal ulcer must be guarded because once this ulcer has developed, the likelihood of recurrence is greater than the incidence of recurrence after treatment of either gastric or duodenal ulcer. It is essential that the patient with the ulcer diathesis be familiarized with the natural tendency of the disease to recur and be instructed in methods adapted to prevent such recurrences. The provocative influences active in many cases include nervous tension, anxiety and mental conflict, fatigue, upper respiratory infections and the ingestion of drugs irritating to the gastric mucosa. The basic regulations of the ulcer regime must always prevail and with the earliest indication of recurrence, the very strictest ulcer regime must be restored. In a significant way the skill of the surgeon and the choice of procedure will affect the prognosis and incidence of recurrence of gastrojejunal ulcer.

Summary

1. Gastrojejunal ulcer is the most serious complication of gastric surgery for benign peptic ulcer disease.

2. Diagnosis is possible in nearly all cases through analysis of the history, physical evidence, roentgenologic studies, gastroscopy and gastric secretion.

3. Medical treatment for the marginal ulcer has a selective status even though it offers a maximum of safety and a limited success.

4. The wide use of vagotomy with gastroenterostomy and subtotal gastrectomy is proving incapable of entirely preventing anastomotic ulceration or its complications in the patient with the ulcer diathesis.

5. The patient's personal, historical and clinical record, particularly as to medical treatment, must be meticulously scrutinized before determining on surgical intervention.

6. The surgical procedure and skill must be adaptable to the fundamental principles of pathogenesis and therapy in gastrojejunal ulceration.

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RELATIONSHIP OF THE ESOPHAGUS TO HEARTBURN*

EDWIN BOROS, M.D.

New York, N. Y.

Since the time it first came to the attention of man, the nature, mechanism and mode of origin of heartburn has given rise to considerable speculation and controversy. Various interpretations of this symptom have served to confound this universal complaint into a quagmire of uncertainty and misunderstanding. Used synonymously with hunger pain on the one hand, with a sense of upper abdominal distress or sternal pain on the other, for the purposes of this presentation the word heartburn is interpreted as nothing more than a sensation of burning or sourness in the epigastrium or sternal area. The importance of this symptom is proportionate to its all embracing affliction of both young and old, male and female, irrespective of race, and places it as a spearhead of existent trouble.

Heartburn has many sources of origin, although it appears to be reflected and focussed over a limited and circumscribed area. It can be caused by a disturbed esophagus and more remotely, the stomach, small intestine, large bowel, gallbladder in addition to a deranged nervous system or alteration of glandular activity. Emotion plays a great part in causing and maintaining this symptom. The ingestion of irritants in the form of alcohol, drugs, tobacco, as well as allergic sensitivities all play their part in this picture. While an elevated acid titer of the gastric juice is a most usual accompaniment, a reduced or anacid state may likewise be found existing with a complaint of heartburn. Strangely[1] enough, a patient whose stomach has been completely excised for a carcinomatous ulcer of the cardia, with the jejunum joined to the esophagus, still complained of heartburn after the operation. Kauders[2] and Porges doubt the existence of heartburn in the absence of gastric acid. They attribute negative readings to a failure in technic and suggest that with proper gastric stimulation, these so-called antacid states would be at a different level. They feel that where there is no acid there is no heartburn. While investigators generally agree that the presence of acid induces heartburn, it is felt that a sensitization of the esophageal mucosa is required to initiate and continue the process. The occurrence is described[3] as a simple regurgitation of the gastric contents into the gullet. This explanation seems simple enough anatomically and theoretically, but how an emotional circumstance or allergic phenomenon can fit into this picture is another matter, and so the problem becomes somewhat dimmed in the light of this explanation.

It might be well at this point to give consideration to the mechanics of the nervous control of this organ which may serve as a background to its behavior.

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From the Department of Medicine, New York University Post-Graduate Medical School, and the Fourth Medical (N.Y.U.) Division, Bellevue Hospital, and Bronx Hospital, New York, N. Y.

Numerous attempts have been made to clarify the effects of the autonomic nervous system on the behavior of the esophagus. Cannon[4] carried out certain experiments on animals to determine what action severance of the vagi would have on esophageal function. For a period of 24-48 hours after vagal section, the lower end of the esophagus became atonic, followed soon thereafter by the restoration of the normal tone. Knight's[5] conclusions were at variance with that of the previous worker. His results demonstrated that dilatation of the lower end of the tube was observed to persist after vagal section unless the celiac ganglion was removed and with it the sympathetic stimuli. It is well to remember that the esophageal mucosa itself is insensitive to pain[6], in its normal state, as evidenced by the lack of feeling one experiences when swallowing hot or cold liquids, spices, etc. Instrumental pinching of the mucosa does not ordinarily cause complaint on the part of the patient.

Bingham, Ingelfinger, et al[7] observed clinically that the symptom of heartburn was unaffected after autononomic denervation of the stomach. They emphasized that, of significance in such circumstance is the retained intact esophageal innervation. Further thoughts on the question of the trigger mechanism of this symptom found expression in the muscular sensory mechanism of the esophageal wall. Towards this end, small balloons were inserted into the lumen of the swallowing tube. At times, pyrosis was found to ensue. These findings, however, were by no means consistent. Jones and Richardson[8], in employing this method, subjected 29 normal individuals to this procedure. There were 19 resulting victims of heartburn, the rest complaining merely of a feeling of fullness. Acid, alkali, cold water, gastric contents, and barium were then instilled by means of a small tube. Only two-thirds of these subjects responded with complaints of heartburn. Some years later, Bloomfield[9] and Polland covered the same field of investigations. They established that the effect of pressure as induced by the placement of esophageal balloons within the lumen of the gullet resulted in but few instances of induced heartburn. Babey[10] entered this field of study by applying 1 per cent hydrochloric acid directly to the mucosa of persons complaining of this symptom. He was unable to reproduce it by this method. An anatomic basis for pyrosis has found some adherents in the not infrequent presence of ectopic gastric tissue[11].

Of interest in the evaluation of the most frequent sources of heartburn is the recognition of the relative occurrence of the gastritides, ulcer, emotional states, hiatus herniae, reflex causes such as gallbladder disease, nor can one dismiss allergy too lightly. A wide array of local esophageal disorders may well initiate this symptom, and while peptic ulcer of the esophagus may not be too frequent, the oft encountered presence of esophagitis cannot be denied. In its acute form[12], it is one of the most common of all lesions of the swallowing tube. The most frequent cause is the ingestion of chemical preparations accidently or with suicidal intent. Alcohol, very hot drinks, or the inordinate use of spices has been known to cause mucosal irritation. Foreign bodies, mechanical instrumental trauma, systemic infections, as well as infections outside the organ may spread into the

TABLE I

48 PATIENTS 50 EXAMINATION

Case	Age	Sex	Duration of Symptoms	Diagnosis	Esophagoscopic examination	Reaction to HCl instillation
D.T.	40	M	2 years	duodenal ulcer	normal	none
B.P.	62	F	5 years	gastritis	normal	none
B.K.	35	F	5 years	gastritis	normal	none
L.H.	42	M	2 years	duodenal ulcer	normal	none
E.P.	59	M	5 years	duodenal ulcer	normal	slight
H.O.S.	45	M	10 years	gastritis	normal	none
J.H.S.	42	M	1 year	gastritis	normal	none
M.S.	54	M	18 years	duodenal ulcer	esophagitis	none
E.L.B.	52	M	18 years	duodenal ulcer	normal	none
P.D.	55	M	2 years	duodenal ulcer	normal	none
P.D.	55	M	2 years	duodenal ulcer	normal	none
P.D.	55	M	2 years	duodenal ulcer	normal	none
M.S.	36	M	2 years	duodenal ulcer	normal	none
D.R.	45	M	6 months	duodenal ulcer	normal	none
E.D.	34	F	3 years	duodenal ulcer	normal	none
L.B.	47	M	10 years	duodenal ulcer	normal	none
A.O.	47	M	10 years	gastritis	normal	none
H.B.	47	M	6 years	duodenal ulcer	normal	none
I.H.	48	M	15 years	duodenal ulcer	normal	none
S.S.	67	M	20 years	duodenal ulcer	normal	none
E.E.	45	F	6 years	gastritis	normal	none
M.F.	34	M	2 years	gastritis	normal	none
H.B	55	M	10 years	gastritis	normal	none
J.L.	25	M	6 years	duodenal ulcer	normal	none
W.B.	40	M	10 years	gastritis	normal	none
H.T.	54	M	5 years	gastritis	normal	none
W.A.L.	46	M	2 years	duodenal ulcer	normal	none
A.C. (Be)	70	M	2 years	gastritis	esophagitis	none
M.R.	67	F	1 year	duodenal ulcer	normal	none
M.O.B.	45	M	few years	duodenal ulcer	normal	none
A.S.	41	M	6 years	duodenal ulcer followed by subtotal gastrectomy and anacidity to histamine	normal	none
I.S.	57	M	4 months	gastritis	normal	none
D.D.	52	M	many years	gastritis gallstones	normal	positive
S.P.	53	M	16 years	ulcer operation 16 years ago	normal	positive
J.D.	53	M	many years	duodenal ulcer	normal	positive
A.F.	64	F	few years	gastric ulcer hiatus hernia oper. 4 years ago hiatus hernia	normal	none
L.S. (Br.)	45	F	many years	hemorrhage probable ulcer	normal	none
C.S.	60	M	7 years	gastric ulcer	normal	none
A.K.	54	M	13 years	duodenal ulcer	normal	none
H.Y.	49	M	4 years	gastric ulcer	normal	none
B.M.	65	F	20 years	gastric ulcer	normal	none

TABLE I (*continued*)

48 PATIENTS 50 EXAMINATIONS

Case	Age	Sex	Duration of Symptoms	Diagnosis	Esophagoscopic examination	Reaction to HCl instillation
D.M.	51	F	4 years	gastritis	normal	none
F.B.	64	F	recent	gastritis	normal	none
B.L.	51	F	1 year	gastritis	normal	none
I.T.	71	M	3 years	hemorrhage hypertrophic gastritis	normal	none
A.S.	63	M	many years	hemorrhage ulcer? gastritis?	normal	none
L.M.	35	M	5-6 years	gastritis	normal	none
L.P.	35	F	cholecystectomy 2 years ago	esophagitis? gastritis?	chronic esophagitis	positive
A.H.	58	M	3-4 years	peptic ulcer	normal	none
M.R.	70	F	many years	chronic gastritis	normal	none

esophagus itself. The chronic type of esophagitis is likewise a common form of esophageal disease.

In order to appraise the changes which might take place within the lumen of the esophagus in patients complaining of pyrosis, a number of patients were studied by inserting the author's flexible esophagoscope[13,14]. By means of direct visual observation changes of the inner lining could be detected. These examinations were carried out on both private and hospital patients. There is no gainsaying that by objective vision, a viewpoint could be established which far exceeds anything that could be obtained by indirect methods. Alterations in mucosal texture and reaction can readily be ascertained, and no guess work is resorted to in the application of local drugs and chemicals. In this study, not only was complete inspection of inner lumen of the swallowing tube readily effected, but dilute hydrochloric acid 1 per cent was applied locally through the instrument by means of an applicator to the lining of the lower third of the organ. Degrees of swelling, redness, erosions, turgescence and tendency to bleeding were noted as well as any other pathology which might come to light. After application of the acid mixture, mucosal changes were likewise looked for, and after withdrawal of the instrument, the patient was queried as to whether his symptom could be reproduced after the local application of acid.

OBSERVATIONS

Fifty esophageal examinations were carried out in 48 different patients. In all of the subjects with the exception of one, hydrochloric acid was present in the gastric contents. The lone exception was a histamine resistant anacidity following a subtotal gastrectomy for duodenal ulcer which failed nevertheless to prevent a recurrence of heartburn. In the total examinations, only three cases of esophagitis were encountered, one in association with a duodenal ulcer, one in a

gastritis and one as an accompaniment of local esophageal inflammation. Of the entire number, five patients showed a positive response to the local application of hydrochloric acid, one being on the basis of an esophagitis.

TABLE II

38 DILATATIONS

Case	Age	Sex	Duration of Symptoms	Diagnosis	Response to dilator
D.T.	40	M	2 years	duodenal ulcer	none
B.P.	62	F	5 years	gastritis	heartburn
B.K.	65	F	5 years	gastritis	none
L.H.	42	M	2 years	duodenal ulcer	none
E.P.	59	M	5 years	duodenal ulcer	slight heartburn
H.O.S.	45	M	10 years	gastritis	heartburn
J.H.S.	42	M	1 year	gastritis	none
M.S.	54	M	18 years	duodenal ulcer	none (has esophagitis)
S.B.	23	M	2 years	duodenal ulcer	none
E.L.B.	52	M	18 years	duodenal ulcer	none
P.D.	55	M	22 years	duodenal ulcer	heartburn
M.S.	36	M	2 years	duodenal ulcer	heartburn
D.R.	45	M	6 months	duodenal ulcer	heartburn
S.G.	61	M	6-7 years	duodenal ulcer	none
E.D.	34	F	3 years	duodenal ulcer	none
L.B.	47	M	10 years	duodenal ulcer	none
H.O.	47	M	10 years	gastritis	none
H.B.	47	M	6-7 years	duodenal ulcer	none
I.H.	48	M	15 years	duodenal ulcer	none
S.S.	67	M	20 years	duodenal ulcer	none
E.E.	45	F	6-7 years	gastritis	none
M.F.	34	M	2 years	gastritis	none
H.B	55	M	10 years	gastritis	none
J.L.	25	M	6 years	duodenal ulcer	none
W.B.	40	M	10 years	gastritis	none
H.T.	54	M	5 years	gastritis	none
J.H.	50	M	25 years	duodenal ulcer	none
M.G.	41	M	20 years	duodenal ulcer	none
M.W.	36	M	20 years	duodenal ulcer	none
C.R.	58	M	4 years	gastritis – gallstones	none
M.K.	24	M	5 years	gastritis	none
J.G.	53	M	16 years	duodenal ulcer	none
W.A.L.	46	M	2 years	duodenal ulcer	none
E.G.	59	F	few years	gallstones	none
A.A.	44	M	few years	gastritis	none
A.M.	33	F	4 years	duodenal ulcer	none
M.M.	37	M	2-3 years	gastritis	none
J.L.	39	M	6 weeks	gastritis – duodenal ulcer	none

Of the 38 dilatations performed (Table II), six patients complained of heartburn after forceable distention of the esophagus. One had an esophagitis, three had duodenal ulcer, and one a gastritis.

Conclusion

Direct inspection of the interior of the esophagus in 48 patients points to the relative infrequency which the esophagus shares in the explanation of the symptom of heartburn. The direct application of hydrochloric acid through the esophagoscope likewise acquits this organ from any especial sensitivity in patients with pyrosis. Mechanical intralumenal pressure seems to suggest that some intramural or nervous factor may be implied in this process. The weight of negative responses leaves much to be desired for a conclusion in its favor. The studies conducted lend credence to the belief that with the exception of local esophageal pathology, the role of this organ in the production of heartburn is minimal.

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EDITORIAL

The Sedimentation Test

An increased blood sedimentation rate indicates, but a normal rate does not exclude the presence of disease.

A measure of the severity of the disease is the rapidity of sedimentation of the red blood cells, and when a level has been established in a given case, this provides a measure of the progress of the disease.

Apprehension on the part of the patient may be a factor in giving erroneous readings. In order to obviate this chance of error, two or more blood sedimentation tests on successive days should be routine procedure. The lower of the two readings is accepted as reflecting the presence or absence of a destructive lesion.

A reliable means of differentiating between benign and malignant lesions of the digestive tract has been long sought for as a diagnostic test. Cancer in its early stages does not necessarily induce an increased sedimentation rate. In a suspected case of cancer of unknown location in the gastrointestinal tract, the patient having been otherwise in a good physical condition, the sedimentation rate was found to be normal. Several months later when additional symptoms were evident, the sedimentation rate was found elevated, thus demonstrating that the test may be unreliable when malignancy is in the incipient stage.

In the differentation between non-malignant and possible malignant ulcer of the stomach, the sedimentation test may be of diagnostic value if the blood cells settle more rapidly than in normal cases. If the settling is rapid, it favors malignant degeneration. Here too, in early cases of cancer, the sedimentation rate may be normal.

In lesions involving the colon, where anemia is present due to bleeding, the sedimentation rate will show increased settling. Clinicians know that the blood picture differs with the location of the lesion and that secondary anemia is more marked with right-sided than left-sided tumors. The right half of the colon is of greater caliber, permitting larger growths to develop with more bleeding surface and a resultant higher grade of anemia. In the right half of the colon, adenocarcinoma is the most common type of neoplasm in contrast to the annular constricting type likely to be found in the descending colon.

Since the rate of sedimentation varies with the degree of anemia, a higher rate would point to a malignant lesion in the cecum and ascending colon. At times, due to this extreme anemia, the blood picture may readily be mistaken for that of pernicious anemia.

Although the sedimentation test alone may not suffice in the differential diagnosis or even demonstrate the presence of any specific disease, nevertheless it serves to warn the physician that disease of some kind is present and therefore this test merits a place in diagnostic surveys.

Samuel Weiss

ABSTRACTS

PATHOLOGY AND LABORATORY RESEARCH

QUANTITATIVE TESTS OF GASTROINTESTINAL FUNCTION: H. Z. Janowitz. Am. J. Med. pp. 465-477 (Oct.), 1952.

Reference is made to a number of current gastrointestinal studies. Histamine is shown to be used in order to determine whether a subject can secrete any hydrochloric acid. The level of parietal and peptic cell activity may be estimated from their output of acid and pepsin under basal secretory conditions. The determination of urinary pepsinogen offers a supplementary indirect approach to peptic cell function. The insulin test can be used to determine the continuity of the gastric vagal innervation. Excretion of lyzozyme parallels the clinical cause of chronic ulcerative colitis. The external secretion of the pancreas can be measured with some accuracy by means of the secretin test. The determination of pancreatic amylase and lipase activity in the blood is useful during the course of acute pancreatitis. Indirect measurement of pancreatic enzyme secretion by means of blood enzyme activity following pancreatic stimulation has not yet been satisfactorily established. The biliary pigment response to secretin is a failry reliable measure of gallbladder function. Only exceedingly primitive methods are available for the study of intestinal transport.

J. R. Van Dyne

HISTOPHYSIOLOGICAL FINDINGS IN ACUTE HISTAMINE INTOXICATION AFTER ORAL ADMINISTRATION: M. Gabe. Arch. mal. app. digest. 41:10. (Jan.), 1952.

Contrary to the opinion generally held, intragastric administration of histamine (300 mg/Kg) to the guinea-pig results in acute intoxication which is rapidly fatal. Histologic study of various organs at several stages of the intoxication reveals lesions, certain of which, such as congestion of the abdominal viscera and cytologic modifications of the digestive glands are the same as occur following injection of histamine. After intragastric administration, splenic contraction occurs only after a period of intense congestion; similarly, the well-known dilatation of the pulmonary alveoli is preceded by extensive congestion of their walls.

Cytologic modifications of the gastric glands (extrusion of secretory granules by the chief cells) occur simultaneously with extensive leucocyte infiltration of the stomach walls. The leucocyte infiltration recalls in its intensity the phenomenon of diapedesis which occurs during the course of normal digestion.

In addition to these histologic modifications, the stomachs of guinea-pigs subjected to direct administration of adequate doses of histamine dihydrochloride show successive stages of ulcer formation, terminating in perforation in all animals surviving for long enough periods of time (4 to 5 hours). The earliest stages of this process are evident in the rupture of subepithelial capillary-arcs and in sloughing exfoliation of the surface epithelium. The glandular region becomes denuded and is attacked by hyperacid and pepsin-rich gastric juice, the secretion of which is stimulated by histamine. The ulcer involves the deeper layers; the parietal cells are more resistant than the duct cells. The *muscularis mocosae* and the muscle layer proper becomes involved during the 4th hour of the syndrome, and perforation, which may be single or multiple, results generally during the 5th hour.

These facts support the concept of a double mechanism, partly vascular and partly peptic, in acute ulcer formation due to histamine.

EFFECTS OF VAGOTOMY ON PANCREATIC SECRETION IN DOGS WITH CHRONIC PANCREATIC FISTULA: E. F. Routley, F. C. Mann, J. L. Bollman, and J. H. Grindlay. Surg. Gynec. & Obst. 95:529-536. (Nov.), 1952.

The purpose of the study was to discover the effects of vagotomy on pancreatic function. It was found that stimuli which provoke the production of copious volumes of pancreatic secretion (through the secretin mechanism) include secretin, histamine, hydrochloric acid, and meals. Epinephrine was the only stimulus which diminished the rate of flow of pancreatic juice in this study. Stimuli which increase enzyme activity

(through the nervous and pancreozymin mechanisms) include pylocarpine, methocholine, olive oil, and psychic stimulation. The three enzymes—amylase, lipase, and trypsin—are secreted in markedly parallel concentrations, regardless of the nature of the stimulus. Alcohol is not a powerful stimulant of canine pancreatic secretion, as opposed to its notorious effects in the human subject. The authors were inclined to favor the hypothesis that the vagus control of pancreatic secretions is that of a tonus mechanism that may augment or inhibit local reflexes. Under the experimental conditions employed in this investigation, in trained dogs, vagotomy produced no significant effects on external pancreatic secretion.

J. R. Van Dyne

LIVER AND BILIARY TRACT

THE DISSOLUTION OF FATTY CYSTS IN PRECIRRHOTIC AND CIRRHOTIC LIVERS OF CHOLINE DEFICIENT RATS TREATED WITH LIPOTROPIC FACTORS: W. S. Hartroft, and E. A. Sellers. Am. J. Pathology 28:387-389, 1952.

Treatment of choline-deficient precirrhotic or cirrhotic rats with lipotropic factors for periods up to three months produced dissolution and eventual disappearance of nearly all pathologic fatty cysts. After restoration of dietary choline to such animals, intracellular lipid appeared within the cytoplasm in the walls of fatty cysts; this was associated with a decrease in the lipid within the cyst-lumina. Fat also left cysts through the biliary or vascular routes in a manner similar to that previously found to occur in choline-deficient rats not treated with lipotropic agents. After cysts had been emptied by any of the mechanisms described, the cells in the cyst wall reassumed the appearance of normal parenchyma. The lumen of the cyst was eventually obliterated. Occasionally cysts remained despite choline therapy and these formed collections of atrophic cells with scanty cytoplasm and pyknotic nuclei. If cysts in many of these stages of disappearance occur in biopsy liver specimens taken from human alcoholics it indicates that the fatty and cirrhotic lesions are actually regressing.

J. R. Van Dyne

THE BROMSULFALEIN APPEARANCE-TIME IN BILE: J. Caroli, Y. Tanasoglu and M. Cohen. Arch. mal. app. digest. 41:623-625 (June) 1952.

The bromsulfalein appearance-time in bile is not a laboratory procedure but a simple clinical method. Its measurement is made by the combination of duodenal intubation with the usual intravenous injection of bromsulfalein (150 mg. per square meter). For this purpose, the biliary fluid is simply collected by siphonage into tubes containing a few drops of 10 per cent sodium hydroxide solution; these tubes are shaken every minute until a reddish-violet color develops. In order for the test to be reliable: (a) the output of biliary juice must be sufficient (about 1 c.c. per minute on an average) and (b) it must contain a detectable amount of bile. Moreover the biliary flow can be stimulated by intraduodenal instillation of novocain or magnesium sulfate.

In normal subjects, the bromsulfalein appearance-time ranges between 5 and 15 minutes. This test is of significant value in uncommon cases of subtotal and yet latent common bile duct obstruction. In these instances (5 cases) not only is the bromsulfalein retained in the blood, but the appearance time of bromsulfalein in bile is very delayed (from 30′ to 50′) despite an apparently normal biliary output. On the contrary, in *cirrhosis of the liver*, the bromsulfalein appearance-time is shortened from 5′ to 8′ (10 cases). Unfortunately, most of the latent common bile duct calculi impair neither the biliary flow, nor the bromsulfalein appearance-time.

The test is diagnostically the most informative in incomplete obstructive jaundice. In hepatitis with jaundice (16 cases) the appearance-time is normal or shortened; exceptions are encountered only when a complete intrahepatic occlusion to the bile flow is present. It is the only reliable test in those cases of hepatitis with biological data of pure biliary stasis (4 cases). The test also retains its value in cirrhosis with jaundice (2 cases).

In the course of jaundice due to incomplete common bile duct obstruction (caused by lithiasis, pancreatitis, choledochitis, postoperative stricture, carcinoma of the papilla major) despite an important biliary output, a marked delay in the appearance-time is however recorded. Of great interest is the

test in case of cholestatic cirrhosis (1 case).

Whether jaundice is present or not, there are two main types of bromsulfalein retention in the blood: (1) retentions by parenchymal hepatic damage associated with a bromsulfalein elimination time normal or shortened; (2) retentions due to common bile duct obstruction with a prolonged bromsulfalein appearance-time in bile.

The bromsulfalein retention due to parenchymal lesion seems related to functional impairment on the vascular side of the hepatic cell, but any particle of the dye reaching the biliary duct system rapidly goes into the duodenum. In cirrhosis, the quickened rate of dye elimination may be due to an increase in the biliary output, to shortening of the liver cell cords and to proliferation of numerous new bile canaliculi; in the course of hepatitis with jaundice, even though one agrees with the authors' hypothesis of mechanical obstruction of the canals of Hering, nevertheless a sufficient number of biliary passages remain open, so that the bile and the dye flow rapidly through biliary ducts, when pressure is low.

In jaundice due to incomplete common bile duct obstruction, the bromsulfalein blood retention is related to functional inhibition of the biliary side of the hepatic cell, because of over-pressure in the excretory system. In that case, this effect is uniformly spread out over the whole hepatic parenchyma, which explains the delay in the appearance-time of the dye in the duodenum.

COMMON DUCT EXPLORATION FOR STONES: F. Glenn. Surg. Gynec. & Obst. 95: 431-438 (Oct.) 1952.

Common duct stones may be considered a complication or sequel of cholelithiasis. Their incidence increases with the duration of biliary tract disease and may be expected more frequently in the older age group. The early surgical interruption of biliary tract disease, while stones are limited to the gallbladder only is perhaps the best prophylactic measure available to prevent the formation of common duct stones. The most effective means of determining their presence and achieving their removal is by common duct exploration. In general, when indicated, such exploration should be undertaken at the time cholecystectomy is done for cholelithiasis, but it should not be regarded as a routine procedure. It is an operation that should only be done by those equipped and prepared to do it with care and thoroughness.

J. R. Van Dyne

PARTIAL HEPATECTOMY: P. Stone, and George Saypol. Surg. Gynec. & Obst. 95:191-200 (Aug.), 1952.

The authors discuss four cases of partial hepatectomy performed for hepatoma, cavernous hemangioma, nonspecific granular, and metastatic carcinoma. These are recorded with a review of recent related articles in the literature. Technical considerations in resection of various portions of the liver are presented.

J. R. Van Dyne

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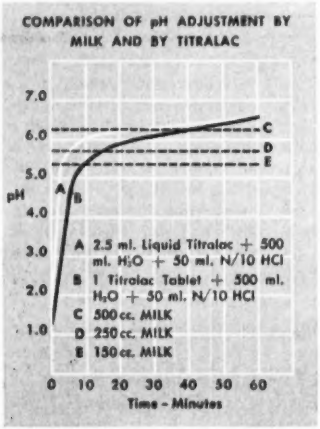

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*Peptic Ulcer. A. C. Ivy, M. I. Grossman and W. H. Bachrach, Blakiston Publishing Co., Phila., 1950.

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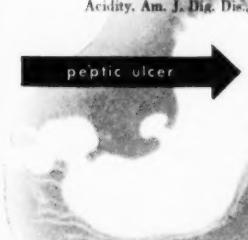
*S. Krasnow, F. Steigmann and L. L. Hardt, Comparison of Effectiveness of Various Antacids on Gastric Acidity. Am. J. Dig. Dis., 17:242 (1950).



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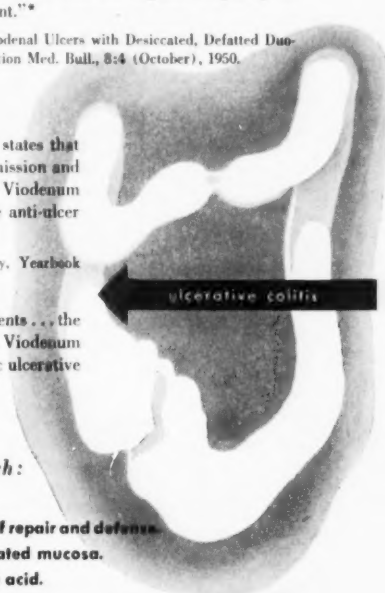
*Medical Management of Gastrointestinal Disorders. Garnett Cheney, Yearbook Publishers, 1950.



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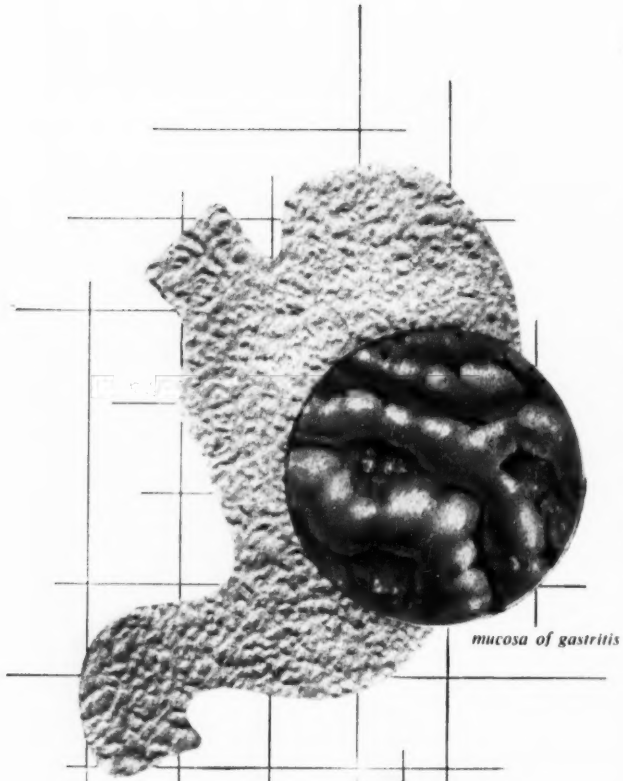

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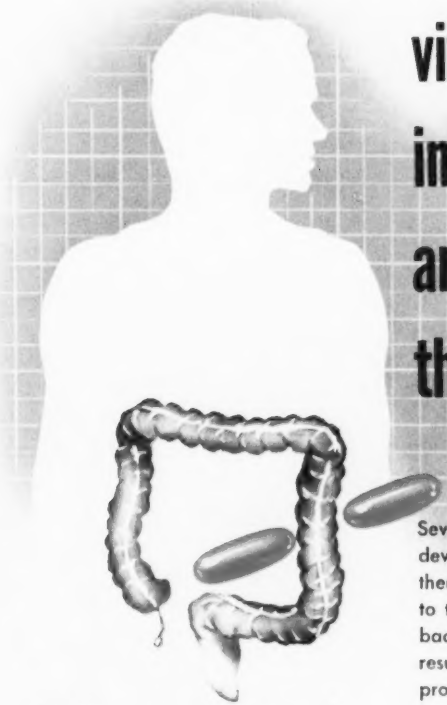

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1. Gewin, H. M., and Friou, G. J.: Yale Jour. Biol. & Med., 23:332, Feb., 1951.

2. Marshall, H. C., Jr., Palmer, W. L., and Kirsner, J. B.: J.A.M.A., 144:900, Nov. 11, 1950.

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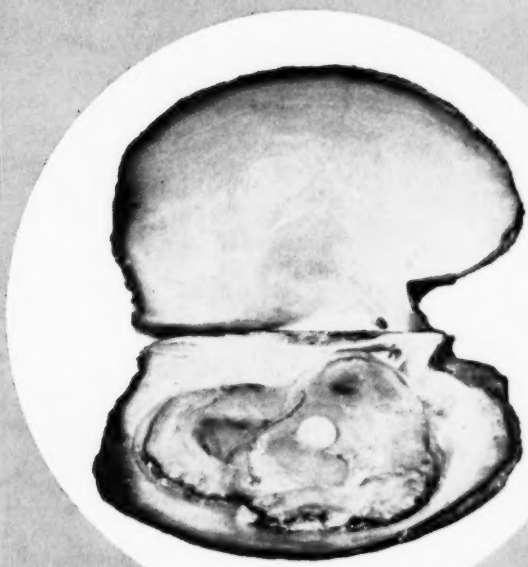

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